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THE OBJECTS OF DIGITALIS THERAPY*†

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ALTHOUGH 143 years have elapsed since Withering[1] first used digitalis consistently in the treatment of heart failure, the situations in which the drug may be expected to be of benefit and the mechanism by which benefit occurs are still subjects of study and investigation.

Before discussing the subject from the present day point of view, let us see what has been the trend of knowledge regarding the use of digitalis in the past. In reviewing the literature of the use of this drug as a therapeutic agent, one finds that rather sharply defined periods are to be recognized: the following are the points of view and contributions which seem to be important.

It is to be expected that the criteria for the use of digitalis should be influenced by the notions which have been current from time to time. Withering made the first contribution[1]. Having found the drug of benefit in certain cases of edema, he advocated its general use as a diuretic. It is to be recalled that at this time Withering was unable to differentiate edema of cardiac origin from that of renal origin. This contribution was later made by Bright. Later still, Kreysig[2] expressed the opinion that digitalis contributed something to the energy of the heart, by which he probably meant that the drug increased the contractile power. He arrived at this notion from studies made in the clinic. Following these observations, the indiscriminate use of digitalis in such diseases as tuberculosis, scarlet fever, measles, and in cases of hemorrhage, caused the drug to fall into disuse. It is due to the next phase in the development of clinical physiology that it was re-established as a therapeutic agent. I refer to the discovery of the method of auscultation by Laennec[3] in 1819, followed by Hope's[4] demonstration in 1831 that closure of the valves gives rise to the heart sounds. Thus it was made possible to diagnose lesions of the

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†Read before the Section of Medicine, The New York Academy of Medicine, Dec. 18, 1928.

valves of the heart, and during the next 75 years it was in the type of valve lesion which was present that we find the criterion for the administration of digitalis. For instance its use was advocated in mitral disease and contraindicated in aortic insufficiency (Corrigan[5]). This remained the situation until 1912. Meanwhile Bouillard in 1835[6] and Traube in 1871[7] had inclined to the use of the drug as a "cardiac sedative." At the beginning of the twentieth century, Krehl[8] and Romberg[9] paved the way for a study of the significance of the behavior of muscle in heart disease, and likewise of the effect of digitalis upon the heart muscle under clinical conditions.

The next advance which exerted an influence upon this problem was the identification by Mackenzie[10] in 1911 of the rhythm of the heart known as auricular fibrillation. The striking effect of the drug in reducing the rate of the completely irregular pulse in this condition together with studies of the effect of the drug on other forms of irregular heart action led physicians to the belief that it was preëminently the irregular heart upon which digitalis acted. This view is still more or less current. So strong was it as late as 1915 that Cohn[11] emphasized the efficacy of the drug in the presence of the normal rhythm when edema was present. Attention was again directed to the action of digitalis on human heart muscle when Cohn, Fraser and Jamieson[12] in 1915 demonstrated changes in the form of the T-wave of the electrocardiogram after giving therapeutic amounts of the drug. In 1924, Dr. Cohn and I[13] showed by means of moving x-ray photographs that digitalis increased the extent of contraction of the ventricles of the human heart, in the presence of a regular rhythm as well as in the presence of auricular fibrillation.

I come next to the question of dosage and standardization. From a vast literature dealing with this phase of the subject, only one contribution of importance can be said to have emerged. I refer to the now well-established fact that large doses of digitalis may be given and that this method of administration is the one of choice. Experience has shown that the biologic assay of the drug by the cat or by the frog method does not parallel the therapeutic effect in patients. The amount, however, of any preparation that is required to give this effect is approximately the same regardless of the age and the weight of the patient. Our experience may be of interest in this connection and illustrates the point I wish to make. We have been using for years a commercial preparation*, 1.0 gm. of which given by mouth within 24 hours may be expected to reduce the ventricular rate in rapid auricular fibrillation to the normal level, to give changes in the form of the T-wave of the electrocardiogram, and in suitable cases to induce diuresis, without the occurrence of such toxic symptoms as nausea and vomiting, and without the occurrence of ectopic

*Digitan (Merck).

beats. It is of small consequence if the effect which is desired is attained when only 0.9 gm. of the drug has been given or that it requires 0.2 or 0.3 gm. more than this amount, since the last doses need not be given or the additional amount may be given in the second 24 hours. In our experience if an effect is not obtained with approximately this amount of the preparation it is of no avail to give larger amounts. Exact information concerning the value of small or so-called "tonic" doses of digitalis is at present lacking.

Since in recent years cardiac output has been so prominent in investigations of the physiology of the circulation, it was to be expected that the effect of digitalis upon this function should be studied. The experiments which Harrison and Leonard[14] and the observations which Burwell, Neighbors and Regen[15] have recently published again focussed attention more keenly on the problem of the action of digitalis. Their observation stands out as one of the important contributions to the study of this drug. They found that soon after the administration of digitalis to normal dogs, the volume output from the heart per minute diminishes. This result was new and unexepected and ran counter to the views which have been built up in part from pharmacological studies in the laboratory and in part from inferences drawn from careful clinical observation. It had been the accepted belief that in the presence of congestive heart failure (edema) the cardiac output per minute was diminished and that improvement consisted in restoring this amount toward its former level. If this view of heart failure is correct, it appears logically to be mistaken practice to prescribe digitalis, which also decreases cardiac output. This situation, as we shall see later, should not be accepted as if all the facts involved in it were known; and we should not draw too far reaching inferences from this observation before other factors have been analyzed.

We have seen therefore in this brief review that the criteria for the use of digitalis viewed in chronological order have been: first, the presence of edema, later its effect on the heart muscle, later still, the presence of certain varieties of valvular disease, and in our own day cardiac rhythm with especial reference to auricular fibrillation, now, a return to its effect on muscle and finally, cardiac output.

In reviewing this subject recently, we were led to ask ourselves: "What are the objects of digitalis therapy?" The supreme object of all therapeutic procedures is to cure the disease completely and, failing this, to alleviate the symptoms, subjective as well as objective, from which the patient suffers. To cure is surely not the object of digitalis therapy; and the situations requiring benefit differ in the several instances in which it is used. Moreover the definition of beneficial action and how its presence is to be ascertained must be

decided. Is action to be judged in terms of an effect, such as its effect on blood pressure or volume output, or is it to be judged by its effect on tone or on contraction or on another of the many actions which it undoubtedly possesses? The answer is, Yes, if any effect goes parallel with benefit. But it does not. Benefit will have to be sought in the net result of all these, in the general reaction of the whole man.

How then, based on what is known of its physiological action, is the administration of digitalis expected to do good? We shall limit the discussion to its use in heart disease and in pneumonia.

In spite of the more or less current view that digitalis is most effective in the presence of auricular fibrillation, experience has shown that the drug is sometimes of benefit to those patients suffering from congestive heart failure in the presence of a normal or regular rhythm of the heart. What the state of the circulation is in this condition in terms of cardiac output is not known. Until recently the view was commonly held that it was decreased. Harrison and Leonard,[14] and Robinson[16] are of the opinion on the other hand that in heart failure the cardiac output may be increased. These authors have recently revived the notion first expressed by Krehl[5] that congestive heart failure is due to imbalance of the two ventricles and that digitalis rectifies this imbalance. There is no direct evidence that this is the mechanism of congestive heart failure, for such an imbalance in output must necessarily be of only short duration. Nor is there evidence for the belief that digitalis can restore balance, since the drug must act equally on the two ventricles. The mechanism by which circulatory efficiency is restored is not at present known.

As has been said, Harrison and Leonard made a significant contribution in the observation that soon after the administration of digitalis the volume output of the heart per minute diminishes. Dr. Cohn and I[17] confirmed this observation; we analyzed this effect further and were able to unravel a twofold action of digitalis. One is on tone of muscle, that is to say, it increases cardiac tone; this causes a decrease in size of the heart, from which issues a decrease in cardiac output. In other words, the heart has been made a smaller pump. A second effect is the action on contraction; the extent of the ventricular contraction is increased. This tends to increase cardiac output. The cardiac output which obtains at any instant is the net result of the working of these two opposing factors. That is to say, cardiac output is a function of size of the heart and ventricular contraction. If cardiac size is not smaller than a critical value, increase in ventricular contraction overbalances decrease in size so that cardiac output increases beyond that initial value. We have also shown that enlarged hearts in dogs without heart failure respond to digitalis in the same manner as do the hearts of normal ones.[18] This is the result one should expect. The question now naturally

arises whether these observations throw light on the way digitalis acts in heart failure in human disease. There is ample evidence in observations made in the clinic that digitalis in therapeutic amounts has an effect on the functions of tone and of contraction in the heart in man. First, with regard to tone, it is well known that an effect of digitalis upon the size of the heart can be demonstrated in heart failure by means of x-ray photographs, that is to say, a decrease in size of the heart occurs. At times this effect can be demonstrated soon after the administration of digitalis; it is however frequently not detected until after prolonged treatment with the drug. With large doses, in normal cases, the effect on cardiac output comes on soon as Burwell, Neighbors and Regen[15] showed. Though the heart does not become smaller, an influence on its size may nevertheless be demonstrated, as was shown by Levy[19] in the case of lobar pneumonia. In this disease enlargement of the heart did not occur or at least tended to take place less frequently if this drug was given. Should the mechanism of heart failure involve decrease in cardiac output, as has until recently been generally believed to be the case, point would be given to what Starling[20] described as the law of the heart. Starling showed in experiments that when heart muscle fibers increased beyond a certain optimal length, decrease in output from the heart resulted. If the optimal or somewhat shorter length were restored, output from the ventricles increased. Heart failure may be a condition in which the fibers are longer than optimal; were digitalis able to restore them to a proper length, that is to say, by exerting its effect on tone, the requirement of the situation would be met. This is the sum of our knowledge with regard to the effect of digitalis on tone. We come next to its effect on contraction. We have ourselves shown that in patients suffering from heart disease, increase in ventricular excursions may take place after the administration of digitalis in therapeutic amounts, even though no demonstrable change in the size of the heart can be seen in x-ray photographs. If increase in contraction occurs without simultaneous decrease in size of the heart, our experiments permit the inference that cardiac output increases. This may be the situation in heart failure in man, but of this there is no direct evidence. We have thought of the mechanism of recovery from heart failure as taking place in such a manner, since it is difficult for us to rationalize improvement and diuresis in congestive heart failure with decrease in cardiac output.

Because of its action in blocking auricular stimuli from reaching the ventricles, digitalis is employed in treating patients suffering from auricular fibrillation with rapid ventricular rate whether congestive heart failure is or is not present. When heart failure is not present, relief from the symptoms due to the rapid ventricular rate is to be expected. When failure is present, one is not surprised to

find that benefit occurs if *failure can be ascribed to the rapid abnormal rhythm alone.* Without doubt, however, its effects on tone and contraction which have already been discussed play a rôle, as in the case where the rhythm is normal. In fact we have devised experiments which show this to be the case in dogs, subjected to artificially induced auricular fibrillation.

I have shown therefore that the only actions of digitalis upon the heart which can at present be demonstrated in patients are effect on tone, effect on contraction, and effect in irregularity. If occasions arise in which these effects are desired, then the use of digitalis is indicated. I have also discussed how heart failure may be influenced by the working of these known actions.

We now come to the subject of digitalis in pneumonia. Its use in this disease at the present time is, in our experience, based on the same three readily demonstrable effects of the drug, all of which can be elicited in the presence of this disease. In the first place it is given for its effect in the presence of auricular fibrillation. During the course of pneumonia, auricular fibrillation and auricular flutter occur as complications which increase in frequency in the age groups beyond 30 years. If patients are under the influence of digitalis when auricular fibrillation begins, a great increase in ventricular rate will not occur, and the circulatory mechanism is not exposed to the strain of rapid auricular fibrillation. In the second place it is given for its effect on tone; we have already made mention of the observation of Levy[19] that the dilatation of the heart which frequently occurs during the course of pneumonia fails to occur if digitalis is administered. Although there is the possibility that dilatation of the heart in pneumonia is a compensatory mechanism, the object first mentioned is sufficiently important in our experience to warrant its being given. And lastly, in addition to its effect in auricular fibrillation and its effect on tone, it is given for its effect on contraction. Cohn has shown that digitalis induces its characteristic effects on the form of the T-wave of the electrocardiogram and on conduction time if the drug is given to patients suffering from pneumonia. If these two effects represent an effect on muscle, as they undoubtedly do, we should expect the drug also to exert its characteristic effect on contraction, that is to say, that it should *increase* contraction.

Harrison and Leonard[14] advise the use of digitalis in this disease on different grounds. They have shown augmented cardiac output in artificially induced pulmonary infection in dogs.[21] They infer that the cardiac output of patients suffering from pneumonia is also increased and that increased cardiac output in this disease is deleterious. They therefore advocate the use of digitalis in order to decrease the volume output from the heart. On the other hand, if increased cardiac output occurs in pneumonia, it may be a compensatory mech-

anism by which the heart responds to anoxemia. In this case to restore cardiac output to a lower level may not be desirable.

I have said that the objects of giving digitalis in cardiac disease are to increase tone, to increase contraction and to elicit its effect in the fibrillating heart, but whether these objects will be attained in terms that can be translated as benefit to an individual patient cannot be foretold. We cannot predict whether good will result from increasing tone, from increasing contraction, or from blocking the auricular impulses in a fibrillating heart. At the present time the test has to be made in each case. Not only are the conditions which regulate the effectiveness of digitalis at one time and its ineffectiveness at another time in the same patient unknown, but also the types of heart failure classified on an etiological, physiological or anatomical basis, which are likely to respond to digitalis, if there is any distinction to be made on this basis, are unknown. We no longer hold to the view current in Corrigan's time that digitalis can be prescribed on the basis of valve lesion. Marvin has recently emphasized the necessity in digitalis therapy of making distinctions on the basis of etiology. For instance, he was of the opinion that heart failure occurring in arteriosclerotic heart disease responded more frequently to treatment with digitalis than did heart failure which was the end-result of rheumatic heart disease. If this observation proves to be correct, how is such a difference to be interpreted? Is it that each of these diseases leaves a different imprint on the heart muscle, which in turn is reflected in the effect of this drug on the muscle? Although digitalis will still give changes in the T-wave of the electrocardiogram that are similar in both instances, the effect on tone and on contraction may be attenuated.

We have seen that the administration of digitalis is still far from being a simple problem. If an irregularity of the heart needs to be controlled, if tone of the muscle needs to be increased, if contraction of the heart needs to be strengthened, then the use of digitalis is indicated. It remains for future study to ascertain precisely how benefit is to be recognized, how benefit occurs, how benefit is to be measured and in what instances benefit is to be expected.

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THE NERVOUS HEART*

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It is fashionable at meetings of cardiologists to discuss various aspects of abnormal structure or function of the circulatory apparatus. I have turned aside and chosen as subject the "nervous heart" for three practical reasons: first, because this is one of the most common if not the most common condition the cardiologist sees; second, because it is the one in which therapy can be most brilliant; and third, because unfortunately it is also the condition most often receiving poor treatment.

The term nervous heart is of course not scientific; but it does serve the useful purpose of designating a group of disturbances in the efferent or afferent (often both) nerves of the heart, caused in many ways, and of which the essential feature in most instances is an anxiety neurosis of greater or lesser severity. The efferent disturbances affect the frequency or force of the heart action, the afferent result in heightened perception of the heart action, pain or other abnormal sensation. Both phenomena commonly occur together through interaction with the mind. For example, there may be increased heart action resulting in increased afferent stimuli and hence mental disturbances; or heightened heart consciousness may cause mental disquietude and thence increased heart action; or fear may initiate the vicious circle.

Etiology.—Both sexes and all ages beyond early childhood are affected, but more commonly young adults and women at the menopause. Sedentary occupations contribute relatively more cases, probably because they attract the less rugged elements of the population. The hereditary neurotic type of constitution is the important predisposing cause. Many such subjects are dextrosinistrals or "cross wired," i.e., if naturally right handed will aim a gun with the left eye or vice versa—a very interesting personality type described by Quinan.[1]

The condition is precipitated by a large variety of factors in the heart itself, in the rest of the body or in the mind. Crippled valves, abnormal heartbeat mechanism and hypertension do not protect against neurosis, but on the contrary may be the starting point for purely neurotic symptoms which are often more important than the organic changes present—important in the practical sense of producing greater suffering and disability and offering greater possibilities for treatment. This is a fact which is inadequately appreciated. All practitioners of medicine, but especially those who treat heart cases, should have at

*Read at the annual scientific session of the American Heart Association, Portland, Oregon, July 9, 1929.

[1]Quinan, C.: Arch. Neurol. and Psych. 7: 352, 1922, and personal communications.

least a superficial acquaintance with the anxiety neurosis, including its formes frustes, and some aptitude for its prophylaxis and treatment.

Precipitating factors in the body outside the circulatory apparatus are in general those which affect adversely general strength, sleep, weight, and quality of blood and other tissues. Many cases appear during convalescence from infections or in the presence of focal infections, after prolonged or excessive effort, etc. Others are associated with disturbance of the gastro-intestinal tract or the ductless glands, especially the thyroid. Tea, coffee, and tobacco in adequate dosage in susceptible persons undoubtedly do produce irritability of the heart, i.e., acceleration, a "bumpy" action, premature contractions, etc., with or without heightened heart consciousness; but such direct effects have been much overrated, and when these substances are effective, it is more often indirectly through interfering with nutrition, sleep, etc. What has been loosely termed the "cigarette heart," cases of the sort we are discussing, constituted the bulk of those referred from the British army to their heart hospital during the war; and analysis showed that, whereas these men were culled from an army of almost universally excessive smokers, they themselves for the most part smoked little or not at all. This finding, of course, is not to be construed as an argument for the protective influence of tobacco, but simply as another testimony to the fact that certain types of persons tend to develop cardiac irritability—the same types that are likely to eschew tobacco and adopt diet fads.

But the most important precipitants are psychogenic. Mental processes, conscious or subconscious, interplay with most, perhaps with all other etiological factors, and are sometimes solely responsible. Many cases develop after business reverses, domestic maladjustment and the like. Modern civilization provides a fertile soil for the growth of psychoneuroses and especially those concerned with the heart. I refer not especially to the familiar "pace at which we live," but rather to the general diffusion of knowledge about the vital function and the diseases of the heart. Valvular disease, high blood pressure and angina pectoris are common fireside topics. Organizations with philanthropic and educational aims such as the American Heart Association stress in the mind of the public the prevalence of heart disease. Such publicity is of course necessary, and I do not criticize the work of this Association; but I do urge that all who have contact with the public through the printed page, the lecture platform or the clinics keep constantly in mind the danger and do the utmost possible to avoid it. It should be emphasized before the public that most "heart symptoms" do not mean heart disease at all, and that those who think they feel them should promptly transfer the responsibility to their medical advisors.

This is the best that can be done, and yet we may as well frankly

admit that the long-suffering common man will often encounter further grief when he follows this advice. For the average medical practitioner still has much to be desired in ability to discriminate between important and unimportant heart signs and symptoms. With a dim understanding of precordial pain, irregular heart action and murmurs, the physician who encounters any such phenomena, even in a patient he believes to have a sound heart will usually add, after a feeble reassurance, the advice to "be careful"; and this may be all that is needed to confirm an incipient neurosis. Or the neurosis may be entirely fabricated out of contact with the doctor, as the following case illustrates:

A young male bookkeeper was found to have a faint functional systolic murmur and frequent ventricular premature contractions. The latter were identified only by careful auscultation and by electrocardiogram. The remainder of the examination, including x-ray of heart, was entirely negative. Symptoms were extreme heart consciousness especially of the "big bump" following the premature contractions, frequent lancinating precordial pain, breathlessness on effort and fatigue all the time, all of which had resulted in idleness for six months and bed rest much of the time. The interesting feature was the onset six months previously. At that time he had been rejected for employment at a hospital because the examining physician had found "heart-block and a heart murmur." The doctor evidently had been vastly interested in his discovery, for he had called one or two other doctors to see it; and after free discussion in the presence of the amazed applicant, they had declined to take him as an employee but graciously accepted him as a patient and put him to bed. The patient admitted that all his symptoms dated from that day and that prior to that time he had led an active life and had never known that he had a heart.

Gross errors in diagnosis are not the only things to be avoided. More common is the overestimation of the gravity of a compensated valvular disease or hypertension and the imposition of ill-advised restrictions in work or recreation. Or again, after a competent internist or cardiologist has made a correct estimate of the physical state of the circulatory apparatus the patient will misinterpret his words or even his silence. I have heretofore described the lawyer who knew that he had hypertension (a very benign hypertension), and who left the consulting room of a new doctor in a state of panic because in testing blood pressure the doctor said nothing but looked wise. That doctor undoubtedly enjoyed the agreeable sensation of psychological devoir skillfully performed. He had carefully avoided uttering any alarming words, and remained naïvely ignorant of the fantastic interpretation which the penetrating lawyer had derived from that wise look. Reflection over this case has given me what I believe is a definite refinement in blood pressure technic. It is to cultivate at the moment of observation a bored expression rather than a wise one; and then if I wish not to announce the reading, to inquire, while the air is yet sissling out of the machine, "How are your bowels?"

SYMPTOMS

Nervous heart symptoms include many of those of organic heart disease and, as has been suggested, are often superadded to heart disease. Anxiety is the most important and usually stands in a mixed relation of cause and effect with the subjective and objective heart phenomena. Among the sensory experiences of patients, heightened consciousness of heart action is most prominent. Usually referred to the precordium, the pulsatile sensation may be complained of in the ears, the neck, epigastrium or extremities. In mild cases, it may be simply an exaggeration of the normal heart action perception associated with effort or excitement; and these patients may find effort limited by this sensation rather than ordinary hyperpnea. Or it may be only the "bump" following a premature contraction which is felt or the regular heartbeats after using tea, coffee or tobacco, or after meals, or on lying down, or when in an elevated altitude. In more severe cases the pulsations are felt under all circumstances.

Often associated with heart consciousness, but at times independent, is the symptom of position aversion. Most normal persons and many with various types of heart disease can lie comfortably on the back or either side. Cardioneurotic patients may have no special preference, but as a rule they do. They object most often to lying on the left side, sometimes the right side or either side or occasionally the back. As reason they describe vague discomfort, increased heart consciousness, smothering sensation or precordial pain. Only occasionally do uncomplicated cases require more than one pillow. That this position aversion as well as heart consciousness in general is a sensory phenomenon rather than due primarily to change in cardiodynamics is suggested by the fact that so many patients with crippled or very large hearts do not show it. One young man with a "cor bovinum" due to aortic insufficiency said that he avoided lying on the left side, not because it gave him the slightest discomfort, but because the action of his heart in that position rocked the bed so violently that his wife could not sleep!

Precordial pain is common. It rarely has the compression quality suggestive of angina pectoris but is usually a dull ache, sore feeling, burning sensation, or a lancinating pain. The latter is occasionally severe, like a knife-thrust, a stroke of lightning, etc., and is often confused with angina. These pains rarely have any close relation to effort, excitement, meals, etc. They may radiate to the left arm or elsewhere. With or without pain there is often precordial sensitiveness to touch, so much so that patients sometimes try to avoid ordinary contact of clothing over the heart, especially the region of the apex.

Other common symptoms are the group associated with the effort syndrome: easy fatigue, breathlessness with slight effort (sometimes failure to obtain satisfaction from a deep breath, without exercise),

increased sweating, especially of the axillae and hands, faintness, tachycardia, and cool, moist and often cyanotic extremities.

PHYSICAL EXAMINATION

Physical examination reveals nothing specifically indicating the nervous heart, for it must be remembered that it occurs in those with diseased as well as normal hearts; and the effort should be rather to detect nervous and especially psychic deviations from normal. In the effort syndrome group will be found the usual tachycardia, poor response to effort, etc. Search should be made for underlying causes such as constitutional inferiority, glandular disturbances and infections.

TREATMENT

Treatment is first of all prophylactic. Remembering the ease with which grave psychic traumata may be inflicted, the intelligent and conscientious doctor will spare no pains to exhibit a salutary conversation and demeanor before the sort of patient who is a candidate for neurosis. He will not as a rule conceal abnormal findings, because the denouement which is likely to follow at a later date will probably be a worse blow than the properly understood facts at the outset. In order to help these patients the doctor must above all things have their confidence, and this will be denied him unless he establishes a reputation for candor. And the plain facts properly understood (and so necessary to be understood if the cardiac patient is to care for himself properly) are rarely so damaging psychologically as the fantastic mental pictures of the patient who feels that his physician is concealing things.

The war experience emphasized the importance of slow resumption of work after infectious diseases and also the frequency of cardiac irritability when men naturally fitted for and habituated to clerking were subjected to heavy physical strain. These lessons should be remembered in civil practice.

For some of the established cases of neurosis, technical psychotherapeutic methods in the hands of experts may be needed. But these are few compared with the great numbers of mild cases where simple encouragement and a suitable regimen, usually involving gradual resumption of activities, are sufficient. Some patients need coaching over a period of time. For others a single interview will effect a cure; but the examination should be extensive enough to make the patient feel that his condition has received adequate investigation. From this point of view x-rays and electrocardiograms are often legitimate therapeutic adjuncts even when they are not considered essential to diagnosis.

(For discussion, see page 115.)

STUDY OF T-WAVE NEGATIVITY IN PREDOMINANT VENTRICULAR STRAIN*

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It has been known for a long time that certain cardiac lesions throw a burden chiefly on the right or on the left ventricle. This has been manifested by the finding at necropsy of hypertrophy and dilatation predominantly of one or the other ventricle. Clinicians are familiar with the evidence of failure of the right or of the left side of the heart: hepatic engorgement and edema of dependent members when the right ventricle has failed, and marked dyspnea and pulmonary edema when the left ventricle has failed.

Early in electrocardiographic studies, certain modifications of the QRS complexes came under careful scrutiny in relation to anatomical preponderance of the right and of the left ventricles. The work of Einthoven, Lewis,[14] Herrmann and Wilson, Pardee,[20] and others, has shown how closely such electrocardiographic changes parallel the actual changes in the size of the right and of the left ventricles. Lewis[15] has summarized the limitations that attend the attempt to evaluate on the basis of electrocardiographic evidence the changes in mass of the right and of the left ventricles that are indicative of preponderance. It is of interest to the present discussion to state that such correlations have a fairly high degree of accuracy when certain exceptions are borne in mind.

Nowhere has the idea been clearly advanced that a relationship may be observed between types of inversions of the T-wave and injury predominantly to the right or to the left ventricle in man. Herrmann and Wilson pointed out that ventricular preponderance does not produce characteristic changes in the T-wave. They suggested, however, that modifications of the T-wave occurring in hypertrophic preponderance of one or the other ventricle may be the result of myocardial changes which accompany most forms of heart disease.

Interest in the study of significant alterations in the T-wave was stimulated by the work of Willius,[26, 28] who showed their importance in relation to prognosis. He found that among patients whose electrocardiograms exhibited significant inversions of the T-wave mortality was double or treble that among comparable cases in which inversion of the T-wave did not occur. In his series of seventy-four patients with hypertension, whose electrocardiograms showed inversion of the T-waves in Lead I or in Leads I and II, the mortality ranged from 70 to 80 per cent, and death occurred on the average in a little less than

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elèven months. In comparable patients of the same sex and age, but without inversions of the T-wave, the mortality varied from 15 to 31 per cent, and death occurred on the average in a little less than thirteen months. In twenty-eight cases[31] of aortic regurgitation in which electrocardiograms showed inversion of the T-wave in Lead I or in Leads I and II, the mortality was 66 per cent as compared with a mortality of approximately 30 per cent in cases with a similar condition but without inversion of the T-waves. Further observations in these and in other cardiac diseases[9, 16, 29, 31] have shown that mortality is greater among those cases in which there is inversion of the T-wave, as compared with those in which such electrocardiographic changes are not observed.

In the daily clinical observation of patients suffering with cardiac lesions which are capable of producing a differential effect on the two ventricles, we have observed certain correlations between the type of inversion of the T-wave and that of the ventricle chiefly affected. In particular, we have been impressed clinically with the fact that in lesions which chiefly affect the left ventricle, inversions of the T-wave, when they occur, usually are found in Lead I or in Leads I and II, whereas in lesions in which the load is thrown predominantly on the right ventricle, inversions of the T-wave, when present, are found chiefly in Leads II and III. This observation led to a more detailed examination of the present material to ascertain the degree of accuracy of this observation.

In the present study, cases were chosen in which electrocardiograms had shown significant inversions of the T-wave* and which presented evidence of pathological changes capable of exerting a differential strain on the ventricles. It was found that only cases in which a detailed pathological study had been made were suitable for this study. This is due to the fact that clinical methods, although usually sufficient to disclose the main lesions of cardiac disease, may fail to identify all the pathological changes that have a bearing on the question of which ventricle is chiefly overburdened. A few cases in which there was inversion of the T-wave were excluded because pathological evidence of cardiac lesions was absent and therefore there was no basis in these cases for predicating more strain on one ventricle than on the other. This group was composed largely of cases of hyperthyroidism.

Definite Hypertension.—There were forty-two patients with definite hypertension and without other cardiac lesions which would modify the effect of the hypertension on the left ventricle (Table I). The average age of the patients was fifty-two and four-tenths years. The average blood pressure in millimeters of mercury was 202 systolic and 131 diastolic. The average cardiac weight exceeded the estimated weight

*Inversion of the T-wave in Lead III alone is not considered significant, and cases in which there were inversions of the T-wave in this lead only, were not included.

TABLE I

CASES OF DEFINITE HYPERTENSION WITH T-WAVE NEGATIVITY

CASE	AGE AND SEX	AVERAGE BLOOD PRESSURE		T-WAVE INVERSION LEADS I OR I-II	VENTRICULAR PREPONDERANCE	WEIGHT OF HEART, GM.		VALVES	PERICARDIUM	CORONARY SCLEROSIS		SIGNIFICANT CEREBRAL, RENAL, AND RETINAL DATA	MISCELLANEOUS
		SYSTOLIC	DIASTOLIC			AT NECROPSY	ESTIMATED NORMAL			RIGHT	LEFT		
3	44 M	211	139	+	Left	Markedly enlarged	422	Negative	Marked hydropericardium	0	0	Extrarenal sclerosis; probably chronic glomerulonephritis	No digitalis given
10	81 M	220	164	(1)* +	None	618	305	Negative	Acute fibrinous pericarditis	1 +	1 +	Arteriolar sclerotic atrophy of kidneys	No digitalis given; second and third electrocardiograms, taken two months later, showed no T-wave changes; hypertrophy and dilatation of left ventricle 2+; hypertrophy of right 1 +; malignant hypertension
14	52 M	135	91	+	None	Much enlarged		Dilatation, of aortic, mitral, and tricuspid rings	Negative				No digitalis given; auricular flutter with 2:1 block; left ventricle markedly thickened, right very thin; marked dilatation of all heart chambers; fatty changes in myocardium
20	28 F	180	130	+	Left	Much enlarged	288	Negative	Negative	0	0	Chronic diffuse nephritis; discs blurred; low grade optic neuritis	No digitalis given; marked dilatation of heart; marked fatty degeneration of myocardium
21	61 M	201	114	+	Left	700		Negative	Negative	1 +	1 +	Hemorrhages in brain; right hemiplegia day before death; arteriosclerotic atrophy of kidney	No digitalis given; hypertrophy 3 + and dilatation 2 + of both ventricles

*Numeral in parenthesis signifies the electrocardiogram.

TABLE I—CONT'D

23	42 M	240	140	+	Left	573	300	Slight sclerosis of mitral and aortic	Slight thickening over right auricle	2 +	2 +	Chronic diffuse nephritis	No digitalis given; both ventricles hypertrophied; aortic sclerosis 2 +
31	60 M	220	132	+	Left	524	300	Negative	Negative	2 +	2 +	Arteriosclerotic atrophy of kidneys; arteriosclerosis 2 + with retinitis 2 + of malignant hypertensive type	No digitalis given; left ventricle hypertrophied 3 +, right 2 +; left auricle hypertrophied 1 +; malignant hypertension
32	50 F	168	120	+	Left	525		Sclerosis 3 + of mitral	Negative	3 +	3 +		No digitalis given; exophthalmic goiter also slight myocardial fibrosis; no definite infarction
34	49 F	220	138	+	Left	1.5 times normal size	244	Aortic and mitral leaflets slightly increased in thickness	Negative	1 +	1 +	Advanced renal arteriosclerosis; marked albuminuric retinitis	No digitalis given
45	75 F	154	107		Left	550	275	Negative	Negative	1 +	1 +		First electrocardiogram showed diphasic T in Lead I; 22.5 c.c. digitalis before second electrocardiogram, which showed diphasic T in Lead I and inverted T in Leads II and III; both ventricles dilated
53	60 F	160	107	+	Left	620	354	Negative	Negative	1 +	1 +	Advanced arteriosclerosis of brain with cerebral softening; advanced arteriosclerosis of kidney; fundus oculi negative	Eight c.c. digitalis before first electrocardiogram; hypertrophy of left ventricle; dilatation of both auricles; complete right bundle-branch block
55	68 F	220	138	+	Left	905	414	Negative	Negative	2 +	2 +	Renal arteriosclerosis 3 +; retinal sclerosis of hypertensive type	No digitalis given; uniform hypertrophy of ventricles

TABLE I—CONT'D

CASE	AGE AND SEX	AVERAGE BLOOD PRESSURE: SYSTOLIC	AVERAGE BLOOD PRESSURE: DIASTOLIC	T-WAVE INVERSION LEADS I OR I-II	VENTRICULAR PREPONDERANCE	WEIGHT OF HEART, GM.: AT NECROPSY	WEIGHT OF HEART, GM.: ESTIMATED NORMAL	VALVES	PERICARDIUM	CORONARY SCLEROSIS: RIGHT	CORONARY SCLEROSIS: LEFT	SIGNIFICANT CEREBRAL, RENAL, AND RETINAL DATA	MISCELLANEOUS
60	48 M	195	130	+	Left	705	280	Negative	Negative	3 +	3 +	Marked thickening of renal vessels; retinal sclerosis 3 +	No digitalis given
68	59 M	260	150	+	Left	680	377	Negative	Negative	2 +	2 +	Arteriosclerotic kidneys; marked retinal arteriosclerosis	No digitalis given; left ventricle markedly dilated and hypertrophied 4 +
71	60 M	142	104	+	Left	730	428	Negative	Negative	1 +	1 +		Eight c.c. digitalis before electrocardiogram; hypertrophy and dilatation of left ventricle 2 +
72	45 M	228	140	+	Left	750	422	Negative	Negative	2 +	2 +	Arteriosclerotic kidneys; retinal changes of malignant hypertension	Four c.c. digitalis before electrocardiogram; markedly thickened left ventricle.
78	40 F	250	130	+	Left	565		Negative	Negative	2 +	2 +		No digitalis given; left ventricle wall 2 cm. in thickness
81	35 M	200	150	+	None	490	278	Negative	Acute fibrinous pericarditis (terminal)	2 +	2 +	Chronic nephritis with thickened vessel walls; retinitis of nephritis	No digitalis given
85	63 M	175	120	+	Left	807	300	Negative	Negative	1 +	1 +		No digitalis given; hypertrophy 2 + and dilatation of all chambers

TABLE I—CONT'D

91	58 M	203	111		Right Ch'gd to Left	348	353	Slight arteriosclerotic puckering of mitral valve	Negative	2+	2+	Mild retinal arteriosclerosis of hypertensive type	First electrocardiogram normal; 18 c.c. digitalis two months before second electrocardiogram (further digitalis?); second and third electrocardiograms showed T-wave inversion in Lead III, fourth showed diphasic T in Lead I; moderate hypertrophy of left ventricle; anginal symptoms; some fibrous replacement of muscle in posterior surface of left ventricle
97	62 M	150	110	+	Left	648	363	Negative	Negative	2+	2+		First electrocardiogram showed inverted T in Leads I and II, second showed diphasic T in Lead III, third showed inverted T in Leads III (last 2 were taken after 18 c.c. digitalis, during digitalis intoxication); mural thrombosis left auricle; hypertrophy of both ventricles; marked dilatation of right auricle and ventricle
101	64 M	260	180	+	Left	825	490	Negative	Negative	2+	2+	Arteriosclerotic atrophy of renal vessels	Electrocardiogram after 4 c.c. digitalis; hypertrophy and dilatation of left ventricle
102	66 M	180	105	+	Left	845	451	Negative	Negative	1+	1+		Electrocardiogram after 6 c.c. digitalis; right bundle-branch block; QRS = 0.18 second; markedly dilated left ventricle; paroxysmal dyspnea
103	50 M	220	140	+	Left	623	323	Negative	Pericardium thickened but not obliterated (terminal)	2+	2+	Arteriosclerotic renal vessels; retinal arteries much reduced in caliber with edema of discs 2+	*No digitalis given; left ventricle 3 cm. thick, right 1.7 cm.; malignant hypertension*
110	55 F	255	150	(2+)	Left	516	396	Negative	Negative	1+	1+		Some digitalis taken before first electrocardiogram; normal T-waves in first, 10.5 c.c. digitalis before second; arborization block; QRS = 0.16 second: paroxysmal dyspnea

TABLE I—CONT'D

CASE	AGE AND SEX	AVERAGE BLOOD PRESSURE: SYSTOLIC	AVERAGE BLOOD PRESSURE: DIASTOLIC	T-WAVE INVERSION LEADS I OR I-II	VENTRICULAR PREPONDERANCE	WEIGHT OF HEART, GM.: AT NECROPSY	WEIGHT OF HEART, GM.: ESTIMATED NORMAL	VALVES	PERICARDIUM	CORONARY SCLEROSIS: RIGHT	CORONARY SCLEROSIS: LEFT	SIGNIFICANT CEREBRAL, RENAL, AND RETINAL DATA	MISCELLANEOUS
121	36 F	230	160	+	Left	415	284	Negative	Negative	2 +	1 +	Retinal sclerosis; second stage hypertension	No digitalis given; malignant hypertension; thrombi in auricles and apex of left ventricle
124	54 M	250	150		None	452	271	Negative	Negative	2 +	2 +	Marked thickening of renal vessel walls	No digitalis given; T-wave inverted in Leads I, II, and III
126	42 M	152	109	+	Left	792	343	Slight thickening of mitral valve (atheroma)	Small area of acute fibrinous pericarditis	1 +	1 +		No digitalis given; both pleural cavities obliterated; adhesions of pericardium with diaphragm; incomplete bundle-branch block; QRS = 0.11 second
131	29 F	210	120	+	Left	450	196	Negative	Negative	0	0	Renal arteriosclerosis; retinal arteries small but not sclerosed; retinitis of chronic nephritis	No digitalis given
139	52 F	180	120	+	None	366	245	Negative	Negative	1 +	1 +	Greatly thickened renal vessels; slight retinal arteriosclerosis	No digitalis given; marked dilatation of right ventricle with mural thrombosis
140	37 F	254	172		None	540	217	Negative	Negative	1 +	1 +	Marked renal arteriosclerotic thickening; stage 3 of malignant hypertension with retinitis 3 +	No digitalis given; T-wave inverted in Leads I, II, and III; moderate hypertrophy of left ventricle

TABLE I—CONT'D

143	48 M	180	140	+	None	403	225	Negative	Old adhesive tags anterior surface (slight adhesive pericarditis)	1 +	1 +	Arteriosclerosis with softening of the central nervous system; retinitis of essential hypertension or nephritic type	No digitalis given; dilatation 3 + of left ventricle and 2 + of right; blood urea 224
145	47 M	200	128	+	Left	820	371	Negative	Negative	1 +	1 +	Marked fibrosis of renal vessels; retinitis of malignant hypertensive type graded 2-3	No digitalis given; dilatation of left ventricle
147	65 F	165	120	+	Left	684	300	Negative	Negative	2 +	2 +	Renal blood vessel walls thickened	Seven and five-tenths c.c. digitalis before first electrocardiogram; complete right bundle-branch block; hypertrophy chiefly of left ventricle
158	22 M	190	156	+	Right	474	300	Right coronary and noncoronary cusps are bound together with thickening of commissures	Negative	1 +	1 +	Syphilis of the central nervous system; sclerosis; cerebral hemorrhage; renal arteriolar sclerosis; retinitis of malignant hypertensive stage 2-3	No digitalis given
165	45 M	204	164	+	None	505	300	Negative	Negative	1 +	1 +	Marked sclerosis of renal vessels; retinitis 2 +; malignant hypertension	Eight c.c. digitalis before electrocardiogram; hypertrophy and dilatation of left ventricle
166	52 M	228	150	+	Left	700	325	Negative	Negative	2 +	2 +	Renal arteriosclerotic atrophy; retinal arteriosclerosis 3 +	No digitalis given; hypertrophy of both ventricles but chiefly of left

TABLE I—CONT'D

CASE	AGE AND SEX	AVERAGE BLOOD PRESSURE: SYSTOLIC	AVERAGE BLOOD PRESSURE: DIASTOLIC	T-WAVE INVERSION LEADS I OR I-II	VENTRICULAR PREPONDERANCE	WEIGHT OF HEART, GM.: AT NECROPSY	WEIGHT OF HEART, GM.: ESTIMATED NORMAL	VALVES	PERICARDIUM	CORONARY SCLEROSIS: RIGHT	CORONARY SCLEROSIS: LEFT	SIGNIFICANT CEREBRAL, RENAL, AND RETINAL DATA	MISCELLANEOUS
167	39 F	250	160	+	Left	435	250	Mitral valve thickened slightly with a little puckering and a pin-point hemorrhage	Negative	1 +	1 +	Renal arteriosclerosis; retinal arteries irregularly contracted	No digitalis given
168	56 M	155	105	+	Left	474	300	Fusion of commissures of aortic valve	Negative	2 +	2 +	Reduced caliber of retinal vessels	No digitalis given
169	61 F	230	110	+	Left	435	275	Negative	Negative	2 +	2 +	Encephalomalacia; primary contracted kidney; retinal arteriosclerosis 1 +	No digitalis given; first electrocardiogram showed diphasic T in Lead I, second inverted T in Lead I-II
177	70 M	180	90	+	Left	760	375	Negative	Negative	1 +	1 +		Four and five-tenths c.c. digitalis before electrocardiogram; complete right bundle-branch block; QRS = 0.14 to 0.16 second; hypertrophy 3 + of left ventricle and 2 + of right; dilatation 2 + of right ventricle
182	67 M	160	80	+	Left	712	373	Negative	Negative	1 +	1 +	Enlarged kidneys	No digitalis given; hypertrophy of both ventricles

of the normal heart by 280 gm.* In thirty-eight cases (90.5 per cent) the T-wave was inverted in Lead I or in Leads I and II. In two cases the T-wave was inverted in Leads II and III, and in each of these the T-wave was diphasic in Lead I.

In one of these two cases there were four electrocardiographic tracings, only one of which showed significant inversion of the T-wave. Eighteen cubic centimeters of the tincture of digitalis was given before the second electrocardiogram was made, but it could not be determined whether further digitalis was given before the fourth and significant tracing. In the other case the inversion of the T-wave in Leads II and III followed treatment with digitalis.

Certain observations to be made later in this study, together with observation of electrocardiographic changes observed in patients to whom digitalis is being administered, strongly suggest that this drug has a tendency to cause inversion of the T-waves in derivations II and III, a change which, as we shall observe later, is the same as that observed in conditions producing strain predominantly on the right side of the heart. In two cases, the T-wave was inverted in Leads I, II, and III. This group may include certain cases in which the inversion in Lead III is not of abnormal significance; if so the significant inversion is that in Leads I and II. Repeated electrocardiographic tracings often will show that the T-waves are not actually inverted in all leads and that the significant inversion is either in Leads I and II or in Leads II and III.

Probable Preexistent Hypertension.—Thirteen patients were classified as probably having had hypertension (Table II). This classification was determined largely on the basis of the size of the heart, evidence of previous cerebral vascular accidents, presence of abnormalities in the ocular fundus indicative of arteriosclerosis or of the occurrence of marked renal vascular injury in cases in which determinations of blood pressure indicative of definite hypertension were lacking. The average age of the patients was fifty-eight and two-tenths years. The average blood pressure was 139 mm. systolic and 83 mm. diastolic. The weight of twelve hearts was known, the average of which was 607 gm. The average cardiac weight exceeded the estimated normal cardiac weight by 258 gm. The T-wave was inverted in Lead I or in Leads I and II in thirteen (100 per cent) of the cases.

From a study of the combined group of patients, with definite or probable preexistent hypertension, it was observed that inversions of the T-wave in Lead I or in Leads I and II occurred in 93 per cent.

Definite Hypertension With Marked Coronary Sclerosis.—The condition in nine patients was classified as definite hypertension with marked coronary sclerosis (Table III). The average age of the patients was

*The estimated normal cardiac weight was calculated according to the tables prepared by Smith.[25]

TABLE II

CASES OF PROBABLE PREEXISTENT HYPERTENSION WITH T-WAVE NEGATIVITY

CASE	AGE AND SEX	AVERAGE BLOOD PRESSURE		T-WAVE INVERSION LEADS I OR I-II	VENTRICULAR PREPONDERANCE	WEIGHT OF HEART, GM.		VALVES	PERICARDIUM	CORONARY SCLEROSIS		SIGNIFICANT CEREBRAL, RENAL, AND RETINAL DATA	MISCELLANEOUS
		SYSTOLIC	DIASTOLIC			AT NECROPSY	ESTIMATED NORMAL			RIGHT	LEFT		
1	57 F	170	60	+	Left	515	405	One calcified plaque in aortic cusp	Negative	1 +	1 +	Hemiplegia; sclerosis 2 + of cerebral vessels; fundus oculi negative	Digitalis eight days before coming to the clinic; aorta sclerosed 2 +; exophthalmic goiter; diagnosis of probable hypertension based on heart weight; stroke 3 years ago, and twenty-four hours before death
26	56 M	120	95	+	Left	Marked enlargement		Negative	Negative			Recently formed white infarction of the kidney	No digitalis given; right bundle-branch block; size of heart suggestive of hypertension; marked hypertrophy of left ventricle; marked dilatation of all heart chambers and valve rings
50	51 M	120	98	+	Left	682	300	Negative	Slight adhesions	0	0		No digitalis given; dilatation of left ventricle
58	52 F	191	94	+	Left	500	276	Small vegetations; aortic valve 1 mm. in diameter	Negative	1 +	1 +	Renal blood vessels thickened 3 +; considerable consecutive arteriosclerosis of the retinal vessels	No digitalis given; marked hypertrophy of left ventricle; aortic sclerosis 3 +
76	73 F	180	94	+	Left	366	288	Thickening of medial leaf of mitral valve; no stenosis	Negative	2 +	2 +	Reduction in caliber of arteries and senile fibrosis of the fundus oculi	No digitalis given; no myocardial fibrosis except a little in anterior papillary muscle of left ventricle; moderate thickening of wall of left ventricle

TABLE II—CONT'D

79	63 F	135	95	+	Left	400		Acute terminal mitral endocarditis	Acute terminal pericarditis				No digitalis given; probable hypertension based on heart size and on absence of pericardial adhesions and enough mitral disease; blood pressure also suggestive; left ventricle dilated 3+
80	54 M	140	80	+	Right	570	451	Negative	Negative	1+	1+		No digitalis given; diagnosis on basis of heart size and absence of coronary sclerosis or valve or pericardial lesion; all heart chambers dilated 3+
111	68 M	102	70 (?)	+	Left	922	350	Negative	Negative	0	0	Narrowing and occlusion of renal arteries	Two c.c. of digitalis before electrocardiogram; left ventricle especially dilated
132	57 M	112	85	+	Left	657	270	Negative	Negative	2+	2+	Contracted scarred kidney; extensive arteriosclerosis	No digitalis given
144	59 M	170	88	+	Left	545	325	Negative	Negative	2+	2+	Sclerosis 3+ of renal vessels; sclerosis 2+ of retinal arteries; hemorrhagic type of retinitis	No digitalis given
172	46 M	110	95	+	Left	784	300	Mitral negative	Pericarditis over right auricle	2+	2+		Ten and five-tenths c.c. digitalis before first electrocardiogram; incomplete bundle-branch block; relatives said patient had previous history of hypertension; hypertrophy and dilatation of both ventricles and left auricle
176	54 M	128	58	+	Left	656	500	Negative	Negative	2+	2+		No digitalis given
178	67 M	140	65	+	None	685	377	Negative	Negative	1+	1+	Sclerosis 1+ of retinal arteries	No digitalis given; blood urea 164; hypertrophy and dilatation 2+ of left ventricle and 1+ of right

TABLE III

CASES OF DEFINITE HYPERTENSION AND DEFINITE CORONARY SCLEROSIS

CASE	AGE AND SEX	AVERAGE BLOOD PRESSURE		T-WAVE INVERSION LEADS I OR I-II	VENTRICULAR PREPONDERANCE	WEIGHT OF HEART, GM.		VALVES	PERICARDIUM	CORONARY SCLEROSIS		SIGNIFICANT RENAL AND RETINAL DATA	MISCELLANEOUS
		SYSTOLIC	DIASTOLIC			AT NECROPSY	ESTIMATED NORMAL			RIGHT	LEFT		
13	69 M	144	80	+	Left	522	369	Arteriosclerosis 1+ of aortic; no fusion of valve cusps	Negative	4+	4+	Sclerosis 1-2 of retinal and choroidal arteries	No digitalis given; auricles dilated 2+; paroxysmal dyspnea; slight fibrous streaking of myocardium
19	67 M	184	86	+	Left	646	382	Slight arteriosclerotic changes of valves	Negative	3+	3+	Pyonephrosis with stones; examination of the fundus oculi not satisfactory	Eight c.c. digitalis before electrocardiogram; slight fibrous streaking; no definite infarction; sclerosis 3+ base of aorta; also had elevated urea and low renal function; diffuse cardiac hypertrophy
25	61 M	179	125		Left	Markedly enlarged		Fibrous thickening of aortic and mitral leaflets	Negative	3+	3+	Fundus oculi negative	No digitalis given; T-wave inverted in Leads I, II, and III; left ventricle twice normal thickness
31	62 F	240	100	+	Left	Markedly enlarged		Slight fibrous change in mitral and aortic valves	Negative	3+	3+	Walls of the renal vessels thickened; negative fundus oculi	No digitalis given; complete auriculoventricular dissociation

TABLE III—CONT'D

56	60 M	170	110	+	Left	700		Thickening along line of closure of aortic and mitral valves	Negative	3 +	3 +	Marked thickening of renal vessels	No digitalis given; hypertrophy and dilatation of left ventricle
114	73 M	180	100	+	Left	565	284	Sclerotic aortic valve	Negative	3 +	3 +	Slight senile arteriosclerosis of fundus	No digitalis given; third electrocardiogram showed T-wave inversion in Leads I or I-II; as did second and fifth in Leads I-II-III; no T-wave changes in first and fourth; nodal tachycardia preceded last tracing
134	56 F	220	124	+	Left	672	351	A little atheroma aortic and mitral	Negative	2 +	2 +	Arteriosclerotic changes in the kidney; left homonymous hemianopia	No digitalis given; thrombus in left auricular appendage; angina pectoris clinically; diffuse fine fibrous streaking throughout left ventricle
173	59 F	165	115	+	Left	402	275	Negative	Negative	3 +	3 +	Retinal sclerosis 2 + of hypertensive type	No digitalis given; both coronaries practically occluded in places; clinically angina pectoris; occasional fibrous streaking of myocardium
183	52 M	154	102	+	Left			Not reported	Negative	3 +	3 +		No digitalis given; hypertrophy and dilatation of left ventricle; incomplete bundle-branch block

sixty-two years. The average blood pressure was 182 mm. systolic and 105 mm. diastolic. The average cardiac weight in six patients was 584 gm., which exceeded the estimated normal cardiac weight by 252 gm. In eight cases, 88 per cent, inversions of the T-wave in Lead I or in Leads I and II occurred. In one case, at times there were upright T-waves and at other times inversion of the T-wave in all leads. At least one of the tracings in which there was inversion of the T-wave was taken following a paroxysm of nodal tachycardia, and the influence of such an occurrence cannot be positively excluded in the other tracings in which the T-waves were inverted. In the electrocardiogram of one patient there was inversion of the T-wave in all leads.

Probable Preexistent Hypertension With Marked Coronary Sclerosis.—Six patients were grouped as probably having preexistent hypertension with marked coronary sclerosis (Table IV). The average age of the patients in this group was sixty-one and five-tenths years. The average blood pressure was 143 mm. systolic and 86 mm. diastolic. The average cardiac weight was 478 gm., which exceeded the estimated normal cardiac weight by 221 gm. The T-wave was inverted in Lead I or in Leads I and II in five cases (83.3 per cent). In one case, the T-wave was inverted in all leads, but the facts that this phenomenon was preceded by administration of much digitalis and that hitherto the electrocardiogram had been normal indicate that the inversion was produced by digitalis.

In the combined group of patients with definite or probable preexistent hypertension, when this was complicated by marked coronary sclerosis, the T-wave was inverted in Leads I or in Leads I and II in 86.6 per cent of the cases. Comparing this with the group of patients with definite or probable hypertension, without definite coronary sclerosis, it is found that the same changes in the T-wave occur in both groups. Hypertension when accompanied by coronary sclerosis produces changes in the T-wave similar to those found in hypertension alone, unless myocardial infarction is also present.

Syphilitic Aortic Insufficiency.—Eight patients who had syphilitic aortitis with aortic insufficiency had significant inversions of the T-wave (Table V). The average age of the patients was forty-four years. The average blood pressure was 138 mm. systolic and 45 mm. diastolic. The average cardiac weight in five cases was 620 gm., which exceeded the estimated normal cardiac weight by 313 gm. The T-waves were inverted in Lead I or in Leads I and II in six of eight cases (75 per cent). In two cases inversion of the T-waves was found in all leads but the interpretation of these changes was made somewhat difficult because of the administration of digitalis. In the group as a whole, but particularly in the cases uncomplicated by treatment with digitalis, there was a clear-cut tendency to inversion of the T-waves in Lead I or in Leads I and II.

Aortic Endocarditis With Stenosis or Insufficiency.—There were seven cases of aortic endocarditis with stenosis, or insufficiency, or both. The average age of the patients was fifty-five and five-tenths years (Table VI). The average blood pressure was 115 mm. systolic and 72 mm. diastolic. The average cardiac weight was 569 gm., which exceeded the average calculated normal weight by 290 gm. The T-wave was inverted in Lead I or in Leads I and II in five cases (71.4 per cent). There was inversion of the T-wave in all leads in two cases.

In this group, and in the previous group, in both of which there were aortic lesions, eleven (73.3 per cent) of the fifteen patients had inversion of the T-wave in Lead I or in Leads I and II and four in Leads I, II, and III (26.4 per cent).

Aortic Endocarditis With Mitral Stenosis.—In sharp contrast to this group of fifteen patients with aortic lesions, there was a group in which mitral stenosis complicated aortic stenosis or aortic insufficiency (Table VII). There were seven patients in this group, in six of whom the T-waves were inverted in Leads II and III (85.7 per cent). Two of these six patients had received digitalis, in only one of whom did the amount seem adequate to modify the T-waves. The average age of the patients in this group was fifty years. The average blood pressure was 126 mm. systolic and 68 mm. diastolic. The average cardiac weight was 498 gm., which exceeded the average calculated normal cardiac weight by 199 gm.

In combined aortic and mitral endocarditis there is the possibility of overload predominantly of the right or the left ventricle, depending in some measure on the degree of interference with function of the respective valves involved. Willius[30] has shown that the expectancy of life of patients with aortic endocarditis exceeds that of patients with mitral endocarditis by thirteen years. This indicates either that the strain on the heart, and in particular on the right ventricle, is greater from mitral endocarditis than is that on the left ventricle in aortic endocarditis, or that the right ventricle is less able to bear the strain than is the left ventricle. The occurrence of inversion of the T-wave in Leads II and III in patients in whom both aortic and mitral endocarditis are present may be correlated, possibly, with strain predominantly on the right side of the heart.

There was but one case of combined mitral and aortic endocarditis without definite evidence of stenosis or insufficiency of either valve (Table VII). There was perforation of the mitral valve, which may have produced some degree of mitral insufficiency. The T-waves were inverted in all leads in this case. An indeterminate amount of digitalis had been administered in this case before the electrocardiogram was taken.

Hypertension and Mitral Endocarditis.—When hypertension is complicated by mitral stenosis, again a group of cases is found in which the

TABLE IV

CASES OF PROBABLE PREEXISTENT HYPERTENSION WITH DEFINITE CORONARY SCLEROSIS

CASE	AGE AND SEX	AVERAGE BLOOD PRESSURE		T-WAVE INVERSION LEADS I OR I-II	VENTRICULAR PREPONDERANCE	WEIGHT OF HEART, GM.		VALVES	PERICARDIUM	CORONARY SCLEROSIS		SIGNIFICANT CEREBRAL, RENAL, AND RETINAL DATA	MISCELLANEOUS
		SYSTOLIC	DIASTOLIC			AT NECROPSY	ESTIMATED NORMAL			RIGHT	LEFT		
54	52 M	140	80	+	Left	600	142	Aortic valve stiffened; calcification of mitral ring	Negative	2+	2+		No digitalis given; markedly thickened left ventricle; T-wave upright in later electrocardiogram; no infarction
62	69 M	113	74	+	Left	500	249	Extreme calcification of aortic valve cusps, thick cusps at bases of mitral valve	Negative	4+	4+		No digitalis given; angina pectoris clinically; slight diffuse fibrous streaking scattered throughout the left ventricle
63	81 F			+	Left	450	187	Negative	Fine adhesions easily broken almost completely obliterating pericardial cavity	4+	4+	Cerebral hemorrhage; arteriosclerotic scarring of the kidney	No digitalis given; paroxysmal dyspnea; occasional fine fibrous streaking of myocardium

TABLE IV—CONT'D

73	55 F	160	100	+	Left	335		Negative	Negative	3 +	3 +		Four c.c. digitalis before electrocardiogram; no infarction; dilatation of left ventricle; exophthalmic goiter
87	62 M	164	90		Left	627	373	Negative	Several fibrous-like adhesions	3 +	3 +	Enlarged kidneys	Sixty minims digitalis before first and 800 before second and third electrocardiograms; first electrocardiogram normal, second showed inverted T-wave in Leads I-II-III, third diphasic T-wave in Leads I-II inverted in Lead III
109	50 M	139	88	+	None and right	357	333	Atheromatous changes in all valves grade 2 +	Negative	3 +	3 +	Negative cerebral vessels; arteriosclerotic changes in the kidney; marked arteriovenous compression of the fundus oculi	No digitalis given

TABLE V

CASES OF SYPHILITIC AORTIC INSUFFICIENCY

CASE	AGE AND SEX	AVERAGE BLOOD PRESSURE		T-WAVE INVERSION LEADS I OR I-II	VENTRICULAR PREPONDERANCE	WEIGHT OF HEART, GM.		VALVES	PERICARDIUM	CORONARY SCLEROSIS		FUNDUS OCULI	MISCELLANEOUS
		SYSTOLIC	DIASTOLIC			AT NECROPSY	ESTIMATED NORMAL			RIGHT	LEFT		
7	42 F	142	68	+	Left	340		Sclerosis 3+ of aortic	Negative	2+	2+		No digitalis given; hypertrophy of left ventricle 3+; angina due to almost complete occlusion of coronaries at orifices; inverted T-wave in Leads I-II-III in electrocardiogram taken during angina
21	43 F	115	30	+	Left	Heart dilated		Marked sclerosis of aortic and mitral	Petechial hemorrhages on visceral pericardium			Pupils	No digitalis given; some rheumatic history but case considered to be syphilitic aortitis; acute dilatation of heart; Argyll Robertson pupil
37	42 M	132	60	+	Left			Anterior aortic cusp scarred and adherent	Negative	0	0		No digitalis given; hypertrophy and dilatation of left ventricle; patient had angina with hemorrhagic infarction at apex of left ventricle; extensive calcification in origin of aorta

TABLE V—CONT'D

41	35 F	142	0	+	Left			Chronic syphilitic aortitis	Negative	2+	2+	Negative	No digitalis given; dilatation of left ventricle
59	62 M	154	41	+	None	550	341	Aortic ring dilated 3+; terminal vegetations	Negative	0	0		No digitalis given; diffuse cardiac hypertrophy and dilatation
89	52 M	120	84		Left	750	235	Aortic endocarditis with insufficiency (probably syphilitic)	Fibrous adhesions to pericardium and lung	2+	2+		Three c.c. digitalis before first electrocardiogram, and nine c.c. before second; first showed diphasic T-wave in Leads I-II and inverted T-wave in Lead III; second electrocardiogram showed inverted T-wave in Leads I-II-III; angina present, marked aortitis; left ventricle more hypertrophied and dilated than right
112	45 M	160	25		None	700	353	Retraction of aortic leaflets	Negative	3+	3+	Negative	Fourteen c.c. digitalis before second electrocardiogram; first electrocardiogram showed diphasic T-wave in Lead I; second showed inverted T-wave in Leads I-II-III; saccular aneurysm of ascending aorta 9 by 11 cm.; hypertrophy and dilatation of left ventricle
153	32 F	138	56	+	Left	760	300	Aortic insufficiency	Negative	2+	2+	Negative	Digitalis given 3 weeks before coming to the clinic; 6 c.c. digitalis given before first electrocardiogram; aortitis; dilatation of heart 4+

TABLE VI

CASES OF AORTIC STENOSIS AND INSUFFICIENCY

CASE	AGE AND SEX	AVERAGE BLOOD PRESSURE		T-WAVE INVERSION LEADS I OR I-II	VENTRICULAR PREPONDERANCE	WEIGHT OF HEART, GM.		VALVES	PERICARDIUM	CORONARY SCLEROSIS		RENAL VESSELS	MISCELLANEOUS
		SYSTOLIC	DIASTOLIC			AT NECROPSY	ESTIMATED NORMAL			RIGHT	LEFT		
6	46 M	116	66	+	Left	656		Aortic stenosis 4+; small vegetations on mitral	Multiple small subepicardial hemorrhages	0	0		Two drams digitalis three times daily for one month previously; fibrous and fatty changes in heart; aortic valve completely closed
29	10 F	98	77	+	Left	675	215	Marked aortic stenosis	Negative	0	0		Inverted T-wave in Lead I of first electrocardiogram became diphasic on digitalis; second showed diphasic T in Lead I; hypertrophy and dilatation of left ventricle
35	62 M	122	60	+	Left	5 times normal size		Mitral admits five fingers; aortic stenosis and insufficiency; tricuspid admits seven fingers	Negative	0	0	Arteriosclerotic kidney	Right auricle markedly dilated and thinned; left ventricle hypertrophied 4+
82	62 M	105	89		None	646	306	Sclerosis and calcification 4+ of aortic valve	Negative			Arteriosclerotic changes	No digitalis given; inverted T-wave in Leads I-II-III; both ventricles hypertrophied
129	50 M	150	70		None	505	251	Aortic stenosis with calcification	Negative	0	0		No digitalis given; inverted T-wave in Leads I-II-III; hypertrophied left ventricle
142	54 M	100	75	+	None	504	235	Chronic aortic endocarditis with stenosis; slight mitral endocarditis with stenosis	Negative	2+			No digitalis given; greatly hypertrophied left ventricle; right coronary artery enlarged and tortuous
170	74 M	119	70	+	Left	428	388	Definite calcified aortic stenosis; sclerosis of mitral 1+	Negative	2+	2+		No digitalis given; angina clinically

TABLE VII

CASES OF AORTIC INSUFFICIENCY OR STENOSIS AND MITRAL STENOSIS

CASE	AGE AND SEX	AVERAGE BLOOD PRESSURE		T-WAVE INVERSION LEADS II-III	VENTRICULAR PREPONDERANCE	WEIGHT OF HEART, GM.		VALVES	PERICARDIUM	CORONARY SCLEROSIS		MISCELLANEOUS
		SYSTOLIC	DIASTOLIC			AT NECROPSY	ESTIMATED NORMAL			RIGHT	LEFT	
12	39 F			+	None			Marked stenosis of mitral and aortic	Negative	0	0	No digitalis given; marked aortic sclerosis; clinical diagnosis, mitral stenosis
70	53 M	76	46	+	Left	520	329	Marked aortic stenosis; slight tricuspid stenosis; sclerosis of aortic, mitral, and tricuspid; mitral stenosis	Negative	3+	3+	No digitalis given; first electrocardiogram showed diphasic T-wave in Lead I; marked dilatation of left ventricle; arteriosclerotic changes in renal vessels; negative fundus
83	62 M	180	80	+	Right	381	353	Aortic and mitral endocarditis	No adhesions	1+	1+	No digitalis given; exophthalmic goiter probably accounts for blood pressure; diagnosis, mitral stenosis and aortic endocarditis; hypertrophy and dilatation of both ventricles
99	58 M	120	78	+	Right	862	343	Fish-mouth aortic valve stenosis; partial contraction of mitral	Negative			Seven c.c. digitalis before electrocardiogram; generalized cardiac hypertrophy and dilatation
105	36 F	160	70	+	Right	452	225	Mitral stenosis 4+; aortic endocarditis 2+	Negative	0	0	Much digitalis before coming to the clinic; nauseated coupled beats; left auricle tremendously dilated; dilatation 2+ of left ventricle and 1+ of right
127	49 F	100	68	+	Left	250	272	Stenosis of aortic; some mitral stenosis; vegetations on tricuspid	Fibrous adhesions between two layers			No digitalis given; coronary sclerosis at orifice of left coronary
171	55 F	120	70		None	525	275	Aortic and mitral stenosis	Negative	1+	1+	No digitalis given; hypertrophy and dilatation of both ventricles; left auricle dilated 3+; inverted T-wave in Leads I-II
113*	26 M	134	60		Left	478	363	Bacterial endocarditis of aortic and mitral valves, perforation of mitral	Negative	0	0	Electrocardiogram taken before digitalis; dilatation and hypertrophy of both ventricles: inverted T in Leads I-II-III

*A case of aortic and mitral endocarditis without stenosis or insufficiency.

strain may be predominantly in the left or in the right ventricle (Table VIII). In one case the electrocardiographic changes were not constant and that fact together with much treatment with digitalis makes impossible an analysis of the changes in the T-wave. In a second case, *mitral stenosis* complicated systolic hypertension and a slight degree of aortic stenosis; the T-waves were inverted in Leads II and III.

In two cases in which hypertension was complicated by mitral endocarditis, without satisfactory evidence of stenosis or insufficiency, the T-waves were inverted in Lead I or in Leads I and II (Table VIII). In one of these a previous tracing, after administration of digitalis, showed inversions of the T-wave in Leads II and III; this phenomenon changed to inversion of the T-waves in Leads I and II, two and four weeks respectively, after treatment with digitalis had been discontinued.

Cases of Strain Exerted on the Right Side of the Heart.—To obtain cases of uncomplicated lesions which throw definite strain on the right ventricle in which the electrocardiograms show significant inversions of the T-wave is more difficult. First of all, few cases of mitral endocarditis produce significant changes in the T-wave. Mitral endocarditis is notoriously unlikely to exist as an isolated lesion. Administration of digitalis is so universal and thorough in this group that to obtain cases in which its influence can be excluded is difficult. There are certain pulmonic lesions, also, that seem adequate to throw strain predominantly on the right ventricle.

Three cases of mitral stenosis and of mitral stenosis and insufficiency were studied (Table IX). In one of these, in which digitalis was not given, the T-waves were inverted in Leads II and III. In the second case of inverted T-waves in Leads II and III, 15 c.c. of the tincture of digitalis had been administered before the tracing was taken, so that it is impossible to exclude from the interpretation the effect of digitalis. In the third case much treatment with digitalis, both before the patient came to the clinic and while under treatment here makes analysis impossible. In a case of marked mitral insufficiency, uncomplicated by administration of digitalis, inversion in Leads II and III was seen. In two cases of pulmonary disease producing an increased load on the right ventricle, there were inversions of the T-wave in Leads II and III (Table IX). In no instance were the T-waves inverted in Lead I or in Leads I and II. This result is further strengthened by the consideration already given of groups of cases of aortic endocarditis, with and without complicating mitral stenosis. The presence of mitral stenosis is attended by the frequent inversion of the T-wave in Leads II and III; this is in sharp contrast with the changes in the T-wave seen in aortic stenosis alone. In these groups, although they are small, there is a marked tendency to inversion of the T-wave in Leads II and III, which is not in accordance with the electrocardiographic features ob-

TABLE VIII

CASES OF HYPERTENSION AND MITRAL STENOSIS

CASE	AGE AND SEX	AVERAGE BLOOD PRESSURE		VENTRICULAR PREPONDERANCE	WEIGHT OF HEART, GM.		VALVES	PERICARDIUM	CORONARY SCLEROSIS		SIGNIFICANT RENAL AND RETINAL DATA	MISCELLANEOUS
		SYSTOLIC	DIASTOLIC		AT NECROPSY	ESTIMATED NORMAL			RIGHT	LEFT		
88	69 M	220	80	None	471		Aortic cusps adherent for 6 mm.; mitral endocarditis with slight stenosis	Negative	1+	1+	Arteriosclerotic atrophy of the kidney; arteriosclerotic retinitis	T-wave inverted in Leads II-III
95	58 M	138	93	Changes from left to right in last four electrocardiograms	707	350	Marked calcification and puckering of mitral with considerable stenosis; slight aortic calcification	Normal	2+	2+		First electrocardiogram showed diphasic T-wave in Lead I; T-wave inverted in Leads I or I-II of second electrocardiogram; in Leads II-III; in Leads I-II-III of third, fourth, fifth and sixth electrocardiograms; digitalis before first, third, and fourth electrocardiograms; probably a hypertension, dilatation, and hypertrophy of heart; especially right auricle and ventricle
Cases of Hypertension and Mitral Endocarditis Without Stenosis or Insufficiency												
93	49 F	240	130	Left	810		Moderate thickening and vegetations of mitral and tricuspid	Negative	1+	1+	Renal blood vessels markedly thickened	No digitalis given; no clinical evidence of mitral or tricuspid disease; hypertrophy of both ventricles; inverted T-wave in Lead I
118	48 F	160	120	None	375	251	Old mitral endocarditis (no stenosis)	Negative	2+	2+		Digitalis before first electrocardiogram; inverted T-wave in Leads I or I-II of second and third electrocardiograms; in Leads II-III of first electrocardiogram; left ventricle wall thickened

TABLE IX

CASES OF RIGHT HEART STRAIN

CASE	AGE AND SEX	AVERAGE BLOOD PRESSURE SYSTOLIC	AVERAGE BLOOD PRESSURE DIASTOLIC	T-WAVE INVERSION LEADS II-III	VENTRICULAR PREPONDERANCE	WEIGHT OF HEART, GM. AT NECROPSY	WEIGHT OF HEART, GM. ESTIMATED NORMAL	VALVES	PERICARDIUM	CORONARY SCLEROSIS RIGHT	CORONARY SCLEROSIS LEFT	MISCELLANEOUS
								A. Cases of Mitral Stenosis				
155	51 M	130	100	+	Right	472	313	Thickening and vegetation of mitral stenosis	Negative	1+	1+	Digitalis tablets taken three times daily for ten days (elsewhere); we gave 18 c.c. before second electrocardiogram; on digitalis more or less for one year; left auricle dilated 4+ and right 2+; both ventricles 2+; diphasic T-waves in Leads II and III of first electrocardiogram, in Leads I, II and III of second electrocardiogram; right ventricle thicker than left.
161	34 M	120	96	(2) +	Right	429	300	Mitral stenosis 3+	Negative	0	0	No digitalis given; diphasic T-wave in Lead II of first electrocardiogram; inverted T in Lead III; thickened wall of right ventricle; negative fundi
164	33 M	135	104	+	None	707	300	Marked mitral stenosis and regurgitation	Negative	1+	1+	Fifteen c.c. digitalis before electrocardiogram; left auricle dilated 3+; hypertrophy of left ventricle; dilatation 3+ of both ventricles
								B. Case of Mitral Insufficiency				
180	45 F	155	80	+	None	385	342	Mitral thickened with marked insufficiency	Negative	1+	1+	No digitalis given; iso-electric T-wave in Lead I in first electrocardiogram
								C. Cases of Chronic Pulmonary Disease				
36	64 M	95	85	+	Right			Some sclerosis of anterior leaflet of mitral valve	Negative	2+	2+	No digitalis given; fibrosis of lungs; bilateral pulmonary tuberculosis; increased dyspnea and cough for four years; clubbed fingers five years
133	35 M	122	78	+	Right	470		Slight mitral endocarditis, no stenosis	Adhesions, parietal and visceral	1+	1+	No digitalis given; marked dilatation and hypertrophy of right ventricle; thrombosis of both pulmonary arteries (chronic)

served in conditions producing strain predominantly on the left ventricle; this demands study of a larger group of similar cases uncomplicated by treatment with digitalis.

Coronary Sclerosis.—We have discussed earlier in this paper, eight cases of definite coronary sclerosis associated with definite hypertension, and six cases associated with probable hypertension, in which the T-waves were inverted in Lead I or in Leads I and II in 86.6 per cent of cases. Later, thirteen cases with changes in the T-wave, associated with coronary sclerosis and myocardial infarction, will be discussed. We have only two cases of uncomplicated coronary sclerosis with significant changes in the T-waves occurring independently of hypertension or myocardial infarction. This strongly suggests that inversion of the T-wave in coronary disease is seldom seen except when an additional factor, such as hypertension or myocardial infarction, is present. Willius[27] has called attention to the fact that in 66 per cent of his series of cases of angina pectoris there were no significant inversions of the T-wave. We, likewise, in selecting the present cases from our necrospy material had to reject a number of cases of marked coronary sclerosis because significant changes in the T-wave had not been present. In the two cases of uncomplicated coronary sclerosis included in our series the average age of the patients was sixty-two and five-tenths years. The average blood pressure was 128 mm. systolic and 65 mm. diastolic. The average cardiac weight was 356 gm., which exceeded the average normal cardiac weight by 47 gm. In one case the T-waves were inverted in Lead I in association with incomplete bundle-branch block, and in one case the T-waves were inverted in all leads. Digitalis was not a factor in these cases.

Myocardial Infarction With Hypertension.—Twenty-one patients had myocardial infarction associated with definite hypertension (Table XI). Their average age was fifty-four and four-tenths years. The average blood pressure was 170 mm. systolic and 114 mm. diastolic. The average cardiac weight was 579 gm., which exceeded the average calculated weight by 252 gm. In fifteen cases (71.4 per cent) the T-wave was inverted in Lead I or in Leads I and II. In one case the T-waves were inverted in Leads II and III and were diphasic in Lead I. In two cases the T-waves were inverted in Leads II and III. In each of these cases the infarction was found in the posterior surface of the left ventricle. In two cases in both of which there was infarction in the posterior surface of the left ventricle the T-waves were inverted in all leads. There was one case of infarction in the left ventricle, in which the T-wave was inverted in Lead III only. There is little doubt that infarction takes precedence over strain predominantly of one ventricle in determining the type of changes in the T-wave that will be produced.

TABLE X

CASES OF CORONARY SCLEROSIS WITHOUT DEMONSTRABLE INFARCTION

CASE	AGE AND SEX	AVERAGE BLOOD PRESSURE		VENTRICULAR PREPONDERANCE	WEIGHT OF HEART, GM.		VALVES	PERICARDIUM	CORONARY SCLEROSIS			MISCELLANEOUS
		SYSTOLIC	DIASTOLIC		AT NECROPSY	ESTIMATED NORMAL			RIGHT	LEFT	ANGINA	
170	66 M	110	70	None	340	304	Negative	Negative	3 +	3 +		No digitalis given, no infarctions; auricular fibrillation; inverted T-wave in Leads I-II-III
174	59 M	116	60	Left	373	294	Negative	Negative	2 +	3 +	+	No digitalis given; inverted T-wave in Lead I; incomplete bundle-branch block; lumen of anterior descending artery almost occluded; dilatation of left ventricle

Myocardial Infarction With Probable Preexistent Hypertension.—Eleven patients were studied in whom myocardial infarction complicated probable preexisting hypertension (Table XII). Their average age was sixty-two and seven-tenths years. The average blood pressure was 136 mm. systolic and 84 mm. diastolic. The average cardiac weight was 537 gm., which exceeded the average estimated cardiac weight by 209 gm. In seven cases there was inversion of the T-waves in Lead I or in Leads I and II in the electrocardiograms (63.6 per cent). In one case of inversions of the T-wave in all leads, infarction was present in both the anterior and in the posterior portions of the left ventricle. In one case an electrocardiogram showed a shifting type of change in the T-wave; there was infarction of the heart in both the anterior and the posterior portions. In one case inversion of the T-waves in Leads II and III was associated with infarction in the posterior region of the left ventricle. In another case inverted T-waves in Leads II and III were associated with massive, acute infarction in the posterior surface of the left ventricle. Intermittent incomplete bundle-branch block also developed in this case during the patient's illness, and he had a small infarct in the anterior portion of the interventricular septum, in the region supplied by the anterior descending coronary artery.

Myocardial Infarction With Coronary Sclerosis.—Thirteen cases of myocardial infarction associated with coronary sclerosis alone were studied (Table XIII). The average age in this group was sixty-two and six-tenths years. The average blood pressure was 131 mm. systolic and 81 mm. diastolic. The average cardiac weight was 400 gm., which exceeded the average estimated cardiac weight by 58 gm. In seven patients the T-waves were inverted in Lead I or in Leads I and II (53.8 per cent). In five cases there was inversion of the T-waves in Leads II and III, and in each case there was infarction in the posterior portion of the left ventricle and septum, in the area supplied by the right coronary artery. In one case the T-waves were inverted in Leads II and III, and subsequently, in association with infarction in the anterior and the posterior surfaces of the left ventricle, in Leads I, II, and III. Valvular lesions productive of selective strain on either ventricle were not present in these cases. The changes in the T-wave seemed to depend on myocardial infarction. All the cases of myocardial infarction will be considered in a subsequent study of their relation to inversion of the T-wave.

Myocardial Infarction With Miscellaneous Cardiac Diseases.—Seven patients in whom myocardial infarction was associated with miscellaneous cardiac diseases form this group (Table XIV). The average age of the patients was fifty-five years. The average blood pressure was 140 mm. systolic and 93 mm. diastolic. The average cardiac weight was 698 gm., which exceeded the estimated normal weight by 353 gm. In four cases there were inversions of the T-wave in Lead I or in

Table XI

Cases of Myocardial Infarction Associated With Definite Hypertension

Case	Age and Sex	Average Blood Pressure: Systolic	Average Blood Pressure: Diastolic	T-Wave Inversion Leads I or I-II	Ventricular Preponderance	Weight of Heart, Gm.: At Necropsy	Weight of Heart, Gm.: Estimated Normal	Valves	Pericardium	Coronary Sclerosis: Right	Coronary Sclerosis: Left	Significant Cerebral, Renal, and Retinal Data	Angina	Miscellaneous
9	61 M	164	108		Slight right	626	300	Negative	Negative	1 +	1 +			Digitalis elsewhere; 3 c.c. digitalis at clinic before electrocardiogram; old and recent infarction in posterior portions of right and left ventricles and of interventricular septum; inverted T-wave in Leads II-III
16	58 M	178	118	+		478		Fusion of commissures at *base of aortic* leaflets	Negative	2 +	3 +	More than one-half of glomeruli hyalinized; retinitis of *marked* hypertension		No digitalis 17 days before electrocardiogram; chronic infarction of anterior portion left ventricle near apex and near base, also at obtuse margin of left ventricle
27	56 M	200		+	Left	525		Negative	Negative	4 +	4 +			No digitalis given; angina pectoris clinically
38	45 M	150	110	+	Left	700	363	Negative	Negative	3 +	3 +	Fundus oculi negative	+	No digitalis given; occlusion of anterior descending artery with ancient infarction
42	57 M	152	88	+	Left	650	353	Negative	Negative	2 +	2 +		+	No digitalis given; chronic infarction involving anterior surface of left ventricle, septum, and apex
32	52 F	170	135		None	480	248	Chronic mitral endocarditis; no stenosis or insufficiency	Negative	2 +	2 +	Marked renal arteriosclerosis		Eighteen and five-tenths c.c. digitalis before electrocardiogram; old infarction in posterior and anterior portion of left ventricle, more extensive in *latter area*; *inverted* T-wave in Leads II-III

TABLE XI—CONT'D

69	62 M	150	120	+	Left	575	343	Negative	Negative	3 +	3 +	Renal vessel walls thickened; retinal arteriosclerosis of hypertensive type		No digitalis given; infarction of lower anterior aspect of left ventricle and lower portion of posterior part of interventricular septum
86	59 M	140	120		None	425	333	Negative	Negative	3 +	3 +	Many renal glomeruli obliterated; small granular kidney; fundus oculi negative	+	No digitalis given; chronic myocardial infarction anterior surface of left ventricle; diphasic T-wave in Lead I; inverted T-wave in Leads II-III
92	54 M	240	130		Left	690	382	Negative	Negative	3 +	3 +			Six c.c. digitalis before electrocardiogram; chronic infarction of left ventricle; mural thrombus near apex; diphasic T-wave in Leads I-II (depression of S-T interval)
94	54 F	155	109		Right	496	282	Negative	Few fine adhesions parietal pericardium; dense adhesions to posterior surface of left ventricle	4 +	3 +	Moderate retinal arteriosclerosis of primary type	+	No digitalis given before electrocardiogram; infarction of posterior surface of left ventricle; complete occlusion of right coronary; inverted T-wave in Lead III only
107	54 M	160	140	+	None	421		Negative	Negative	2 +	2 +	Died of cerebral embolism; mild hypertension; arteriosclerosis of the fundus	+	No digitalis given; inverted T-wave in Lead I of second and third electrocardiograms; inverted T-wave in Leads I-II-III in first electrocardiogram; acute and chronic infarction of anterior surface of left ventricle

TABLE XI—CONT'D

CASE	AGE AND SEX	AVERAGE BLOOD PRESSURE		T-WAVE INVERSION LEADS I OR I-II	VENTRICULAR PREPONDERANCE	WEIGHT OF HEART, GM.		VALVES	PERICARDIUM	CORONARY SCLEROSIS		SIGNIFICANT CEREBRAL, RENAL, AND RETINAL DATA	ANGINA	MISCELLANEOUS
		SYSTOLIC	DIASTOLIC			AT NECROPSY	ESTIMATED NORMAL			RIGHT	LEFT			
108	58 M	150	100	+	Right	354	304	Negative	Negative	4+	4+	Renal vessel walls greatly thickened	+	No digitalis given; thrombosis of both coronary arteries; electrocardiogram normal before occlusion
115	54 M	158	112	+	Left	700	328	Negative	Negative	2+	3+	Slight sclerosis of renal vessels	+	No digitalis given; occlusion of left coronary artery with myocardial fibrosis of anterior two-thirds of left ventricle; coronary T-wave in Leads I-II
119	55 M	150	104		Left	846	353	Negative	Negative	1+	1+			No digitalis given; T-wave inverted in Leads I-II-III; chronic infarction in posterior surface of left ventricle
120	54 F	196	92	+	Left	475	315	Negative	Fibrinous exudate	1+	1+			No digitalis given; no infarction; thrombus in anterior descending branch of left coronary artery; left ventricle greatly thickened
137	50 M	220	110		None	870	300	Negative	Negative	1+	1+	Sclerosis 2+ of retinal arteries; retinitis of malignant hypertensive type		Much digitalis two months before coming to the clinic; inverted T-wave in Leads I-II-III; chronic infarction of posterior surface of left ventricle

TABLE XI—CONT'D

138	52 F	150	110	+	Left	567	394	Negative	Negative	1+	1+	*Sclerosis 1+ of retinal arteries; retinitis of hypertensive type*		*No digitalis given;* marked thickening of left coronary artery 3 cm. from orifice; chronic infarction of apex of left ventricle
141	46 M	170	130	+	Left	795	290	Negative	Negative	2+	2+	Renal vessel walls thickened		Fifteen c.c. digitalis before electrocardiogram; old infarction at apex and in anterior basal portion of left ventricle; recent infarction in posterior surface of left ventricle
151	38 F	190	120	+	Left	500	302	Negative	Fibrinous adhesions	1+	1+	Sclerosis 1, of retinal arteries with retinitis of benign hypertensive type		Electrocardiogram after 12 c.c. digitalis; acute infarction of anterior wall of left ventricle; wall of left ventricle thickened
159	60 F	185	94	+	None	463	276	Some sclerosis of mitral valves probably old healed endocarditis	Small patch old obliterative pericarditis 1.5 cm. in diameter	1+	1+	Stroke five months before; much arteriosclerotic thickening of the kidney		No digitalis given; infarction of left ventricle; antemortem thrombus of left auricle
181	64 M	142	100	+	Left	525		Sclerosis 3+ of mitral	Negative	3+	3+			No digitalis given; incomplete right bundle-branch block; left coronary artery occluded near origin with some infarction of anterior surface of left ventricle and interventricular septum

TABLE XII

CASES OF MYOCARDIAL INFARCTION ASSOCIATED WITH PROBABLE PREEXISTENT HYPERTENSION

CASE	AGE AND SEX	AVERAGE BLOOD PRESSURE		T-WAVE INVERSION LEADS I OR I-II	VENTRICULAR PREPONDERANCE	WEIGHT OF HEART, GM.		VALVES	PERICARDIUM	CORONARY SCLEROSIS		SIGNIFICANT CEREBRAL, RENAL, AND RETINAL DATA	ANGINA	MISCELLANEOUS
		SYSTOLIC	DIASTOLIC			AT NECROPSY	ESTIMATED NORMAL			RIGHT	LEFT			
39	50 M	157	89	+	Right and left	552	325	Negative	Negative	4+ calcified	4+ calcified	Senile fibrosis of the fundus oculi	+	No digitalis given; also inverted T-wave in Leads II-III; infarction in left ventricle, both anterior and posterior surfaces, as well as infarction of posterior surface of right ventricle
57	58 M	121	81	+	Left	525	382	Negative	Negative	3+	3+	Renal arteriosclerotic changes; fundus oculi negative	+	No digitalis given; marked atrophy with some fibrosis in anterior and apical portions of the left ventricle
67	60 M	138	90	+	Left	598	490	Negative	Adhesion at apex	3+	3+			No digitalis given; chronic infarction at apex and interventricular septum: occlusion of anterior descending branch of left coronary artery
74	49 M	130	98	+	Left	715	343	Negative	Negative	2+	2+	Unconscious for twenty-four hours; renal arteriosclerosis 3+; reduction in caliber of arteries of the fundus		Eight c.c. digitalis before electrocardiogram; old infarction of left ventricle at obtuse margin extending from midventricle to within 2.5 cm. of apex and anteriorly to within 2.5 cm. of anterior interventricular sulcus; infarction midway between anterior and posterior interventricular sulci, all in distribution of right coronary artery; right bundle-branch block

TABLE XII—CONT'D

77	57 M	130	90		Left	520	353	Negative	No adhesions	3 +	3 +		+	No digitalis given; inverted T-wave in Leads I-II-III; old and recent infarctions of myocardium; old one on posterior surface of left ventricle, recent on anterior surface of left ventricle
106	58 M	112	64		None	555	300	Negative	Negative	3 +	3		+	No digitalis given; inverted T-wave in Leads II-III; incomplete right bundle-branch block; extensive recent infarction posterior surface of left ventricle and septum; small region of recent infarction anterior surface of left ventricle and septum near apex
130	77 M	154	82	+	Right	425	313	Negative	Negative	3 +	3 +	Marked renal arteriosclerosis		No digitalis given; chronic infarction in anterior portions of left ventricle and septum
135	76 M	110	82	+	Left	582	294	Negative	Negative	3 +	3 +	Walls of renal vessels thickened		Two c.c. digitalis before electrocardiogram; complete right bundle-branch block; diffuse fibrosis throughout left ventricle in regions supplied by both coronary arteries
150	78 M	135	90	+	Left	318	223	Negative	Negative	3 +	3 +	Renal arteriosclerotic atrophy; arteriosclerosis of the fundus oculi		No digitalis given; chronic infarction in anterior portion of the left ventricle and septum
162	64 F	158	86		Left	500	300	Negative	Practically negative	4 +	3 +	Much pitting of surface of kidney	+	No digitalis given; inverted T-wave in Leads II-III; ancient and recent infarction in area supplied by descending branch of right coronary artery involving posterior surface of left ventricle and right ventricle; abnormally placed interventricular septum
175	63 F	158	68	+	Left	562	288	Negative	Negative	1 +	1 +	Retinal arteriosclerosis		No digitalis given; chronic infarction of posterior surface of left ventricle

TABLE XIII

CASES OF MYOCARDIAL INFARCTION

CASE	AGE AND SEX	AVERAGE BLOOD PRESSURE		T-WAVE INVERSION LEADS I OR I-II	VENTRICULAR PREPONDERANCE	WEIGHT OF HEART, GM.		VALVES	PERICARDIUM	CORONARY SCLEROSIS		SIGNIFICANT RENAL AND RETINAL DATA	ANGINA	MISCELLANEOUS
		SYSTOLIC	DIASTOLIC			AT NECROPSY	ESTIMATED NORMAL			RIGHT	LEFT			
2	54 M	116	86		Left	388	329	Negative	Negative	2 +	3 +			No digitalis given; diphasic T-wave in Lead I; sclerosis of pulmonary artery; infarction of anterior surface of left ventricle and apex
33	41 M	114	60		Right	368	363	Negative	Apex only adherent to heart	2 +	4 +	Renal vessel walls thickened	+	No digitalis given; infarction of posterior surface of left ventricle and apex; inverted T-wave in Leads II-III
43	56 M	120	90	+		400		Aortic cusps sclerosed 2 +	Negative	3 +	3 +		+	No digitalis given; chronic infarction in anterior surface of left ventricle near apex
47	74 M	118	76	+	Left	404	414	Negative	Negative	2 +	4 +			No digitalis given; infarction of apex and lower anterior portion of left ventricle and septum
51	80 F	150	92		Left	431	272	Negative	Negative	3 +	4 +			No digitalis given; diphasic T-wave in Lead I; inverted T-wave in Leads II-III; thrombus 0.5 cm. upper one-third right coronary artery; infarction of posterior surface of left ventricle; electrocardiogram T_1 type
96	70 M	145	55	+	Left	496	384	Slight arteriosclerotic thickening	Negative	3 +	3 +	No definite renal arteriosclerosis		No digitalis given; chronic infarction (?); complete right bundle-branch block

TABLE XIII—CONT'D

104	72 M	128	82	+	None	373	255	Negative	Negative	4+	4+	Marked thickening of the renal vessel walls		Electrocardiogram taken after 11 c.c. digitalis; chronic infarction posterior wall of left ventricle in region supplied by left coronary artery; chronic pulmonary fibrosis (roentgen ray)
117	54 M	152	84		Left	355	392	Negative	Negative	1+	1+		+	No digitalis given; T-wave inverted in Leads II-III; coronary T-wave; old and recent infarction in posterior surfaces of left and right ventricles
125	69 M	100	80		None	295	323	Negative	Negative	2+	2+			No digitalis given; inverted T-wave in Leads II-III; chronic infarctions, extensive fibrosis and thinning of apex and posterior portion of left ventricle
149	57 M	110	75		Right	475		Negative	Fibrous adhesions at base of left ventricle	3+	4+	Arteriosclerotic scarring of the kidney; fundus oculi negative	+	No digitalis given; inverted T-wave in Leads II-III of first electrocardiogram; inverted T-waves in Leads I-II-III of second electrocardiogram; incomplete bundle-branch block; large chronic and recent infarction of anterior surface of left ventricle and chronic infarction of posterior surface of left ventricle; partial left hemiplegia
154	71 M	Not taken		+	Left	300		Negative	Negative	3+	3+	Sclerosis of renal arteries 1+	+	No digitalis given; fibrosis of myocardium; chronic infarction
163	56 M	140	90		None	480		Negative	Negative	4+	+		+	No digitalis given; inverted T-waves in Leads II-III; coronary T-waves; infarction of posterior portion of left ventricle and interventricular septum
179	60 M	148	98	+	Left	434	343	Atheroma of mitral 2+	Negative	3+	3+	Retinal vessels of small caliber	+	No digitalis given; infarction of lateral wall of left ventricle not extending to endocardium or epicardium; incomplete right bundle-branch block

TABLE XIV

CASES OF MYOCARDICAL INFARCTION ASSOCIATED WITH MISCELLANEOUS CARDIAC DISEASES

CASE	AGE AND SEX	AVERAGE BLOOD PRESSURE		DISEASES	T-WAVE INVERSION LEADS I OR I-II	VENTRICULAR PREPONDERANCE	WEIGHT OF HEART, GM.		VALVES	PERICARDIUM	CORONARY SCLEROSIS		RENAL VESSELS	ANGINA	MISCELLANEOUS
		SYSTOLIC	DIASTOLIC				AT NECROPSY	ESTIMATED NORMAL			RIGHT	LEFT			
8	67 M	110	68	Obliterative pericarditis; infarction	+	Right left	475	255	Negative	Completely obliterated	2 +	3 +	Negative	+	No digitalis given; inverted T-wave in Leads II-III; old infarction in anterior portion of left ventricle and apex; more recent infarction in posterior portion of left ventricle; cerebral vessels negative; fundus oculi negative
11	55 M	172	70	Hypertension; aortic stenosis; infarction		Left	543		Marked aortic stenosis	Negative	3 +	3 +			No digitalis given; chronic infarction of posterior one-third of left ventricle; inverted T-wave in Leads II-III; fundus oculi negative
17	66 M	140	100	Hypertension; infarction; obliterating pericarditis	+	Left	1000 +	450	Negative	Obliterating adhesive pericarditis	3 +	3 +	Moderate sclerosis		No digitalis given; infarction of anterior surface of the left ventricle; definite hypertension

TABLE XIV—CONT'D

48	42 M	150	121	Syphilitic aortitis; infarction		Right	630	323	Thickened aortic valve along line of closure	Negative	2+	2+			Inverted T-wave in Leads II-III; 4.5 c.c. digitalis before electrocardiogram; syphilitic aortitis with insufficiency; old and recent infarction in the posterior portion of left ventricle; definite hypertension
49	29 F	100	80	Aortic stenosis; infarction			573		Marked aortic stenosis; mitral thickening without stenosis or insufficiency	Negative	1+	1+	Negative		Inverted T-wave in Leads I-II-III; no digitalis given; chronic diffuse fibrosis in anterior portion of left ventricle; left coronary almost completely occluded at orifice; sudden death
90	58 M	130	70	Infarction; obliterative pericarditis; mitral and aortic endocarditis	+	Left	960	353	Aortic leaflets shortened and thickened; some thickening of mitral cusps	Completely obliterated by adhesions	1+	1+			Digitalis for nine weeks before electrocardiogram (amount ?); chronic infarction of anterior portion of left ventricle anterior to the obtuse angle
116	68 M	210	120	Infarction; hypertension; hemopericardium	+				Negative	Hemopericardium	2+	3			No digitalis given; acute infarction with rupture of the anterior portion of the left ventricle

TABLE XV

MISCELLANEOUS DISEASES

CASE	AGE AND SEX	DISEASE	AVERAGE BLOOD PRESSURE		VENTRICULAR PREPONDERANCE	WEIGHT OF HEART, GM.		VALVES	PERICARDIUM	CORONARY SCLEROSIS		SIGNIFICANT CEREBRAL, RENAL, AND RETINAL DATA	MISCELLANEOUS
			SYSTOLIC	DIASTOLIC		AT NECROPSY	ESTIMATED NORMAL			RIGHT	LEFT		
15	67 M	Marked fibrosis and calcareous aortic ring; calcification of bundle of His with complete heart-block	171	70	Left			Marked fibrosis and calcification of aortic ring; moderate mitral fibrosis	Negative	2+	2+		No digitalis given; inverted T-wave in Leads II-III; right auricle especially dilated; marked sclerosis of aortic valves with calcification; clinical signs of mitral endocarditis with insufficiency; complete heart-block and bundle-branch block
30	68 F	Hypertension; chronic pulmonary disease	180	96	None	Moderate enlargement		Marked aortic valve sclerosis; moderate fibrosis mitral	Negative	2+	2+	Thickened and sclerosed renal vessels	No digitalis given; ten years cough with marked expectoration; bronchiectasis and purulent bronchiolitis; inverted T-wave in Leads II-III
10	37 M	Aneurysm; syphilitic aortitis	126	68	None	650 with aneurysm		Negative	Negative	0	0	Renal arteriosclerosis; fundus oculi negative	No digitalis given; marked torsion and fixation of aorta; no infarction; inverted T-wave in Lead I
11	76 M	Hypertension; aortic stenosis; coronary sclerosis	170	100	Left	775	313	Aortic markedly calcified; slight sclerosis of mitral valve; aortic stenosis	Negative	2+	3+	Walls of renal arteries greatly thickened; senile fundus	No digitalis given; inverted T in Lead I; enormous hypertrophy of left ventricle; left-ventricle wall thickened

TABLE XV—CONT'D

61	48 M	Probable hypertension; pericardial adhesions	106	62	None	700		Negative	Chronic fibrous pericarditis; adhesions to anterior surface	1+	1+	Cerebral embolism; softening of right cerebrum	No digitalis before electrocardiogram; inverted T-wave in Leads I-II-III; alternating right and left bundle-branch block
75	46 F	Mitral stenosis; obliterative pericarditis	134	80	Right	425	198	Fish-mouth mitral stenosis	Completely obliterated	0	0	Cerebral embolus with left hemiplegia	Six c.c. of digitalis a week for two and five-tenths months before last electrocardiogram; inverted T-wave in Leads II-III in third electrocardiogram; first two electrocardiograms showed no T-wave changes; last electrocardiogram taken day of death and after digitalis
100	55 F	Aortic stenosis; chronic pulmonary disease	154	108	Right	384	255	Aortic endocarditis with stenosis 1+	Negative	1+	1+		No digitalis given; inverted T-wave in Leads II-III; healed tuberculosis; pleuritis and lymphadenitis; metastasis to lungs; purulent bronchitis; bronchopneumonia
122	64 M	Aortic stenosis and insufficiency; coronary occlusion	124	68	Left	820	410	Mitral valve cusps are thick; marked aortic stenosis and regurgitation	Negative	2+	2+		No digitalis before first electrocardiogram; 3 c.c. before second; inverted T-wave in Leads I-II; atresia left coronary orifice with occlusion; very little evidence of infarction
123	66 F	Hypertension; aortic stenosis	240	115	Right	509	297	Slight thickening of mitral; marked of aortic with two cusps joined	Few adhesions anteriorly	1+	1+	Moderate renal arteriosclerosis	No digitalis given; inverted T-wave in Lead I; markedly thickened left ventricle

TABLE XV—CONT'D

CASE	AGE AND SEX	DISEASE	AVERAGE BLOOD PRESSURE		VENTRICULAR PREPONDERANCE	WEIGHT OF HEART, GM.		VALVES	PERICARDIUM	CORONARY SCLEROSIS		SIGNIFICANT CEREBRAL, RENAL, AND RETINAL DATA	MISCELLANEOUS
			SYSTOLIC	DIASTOLIC		AT NECROPSY	ESTIMATED NORMAL			RIGHT	LEFT		
128	40 M	Obliterative pericarditis; mitral stenosis	150	65	Right	With pericardium 800	284	Fish-mouth stenosis of mitral; thickening of aortic; somewhat fused cusps	Adhesive pericarditis	1 +	1 +		No digitalis given; inverted T-wave in Leads II-III; hypertrophy and dilatation of left ventricle
136	58 F	Mitral stenosis; obliterative pericarditis	115	80	None	With pericardium and part of mediastinum 287	272	Fish-mouth mitral stenosis 3 +; insufficiency 1 + with recent vegetations	Completely obliterated by fibrous adhesions	1 +	1 +	Multiple embolic infarctions with cerebral hemiplegia; renal arteriosclerotic changes 2 +	Digitalis for two weeks before electrocardiogram; inverted T-wave in Leads I-II; auricular fibrillation
140	36 M	Tuberculous pericarditis with effusion	108	88	Left		353	Negative	Pericardium thickened, adherent over auricles and great vessels	0	0		No digitalis recorded; T-wave inverted in Leads II-III

TABLE XV—CONT'D

148	61 M	Aortic sclerosis; mitral endocarditis without stenosis or insufficiency	164	68	Left	313		Chronic mitral endocarditis with subacute exacerbation; no stenosis or insufficiency	Negative	2+	2+	Renal lesions negative	No digitalis given; inverted T-wave in Leads I-II-III; aortic sclerosis 4+ with marked dilatation of the aortic arch
152	68 F	Obliterative pericarditis; aortic insufficiency; mitral endocarditis	130	70	Right	550	250	Aortic valve irregularly puckered from sclerosis; mitral similarly affected; aortic insufficiency	Obliteration of pericardial cavity	1+	1+		Twelve c.c. digitalis before electrocardiogram; inverted T-wave in Leads II-III; polyserositis (Pick's disease)
156	56 M	Definite hypertension; obliterative pericarditis	180	110	Left	800	350	Negative	Fibrous pericarditis almost obliterating	2+	2+	Thickened renal vessels; retinitis of glomerulonephritis; reduced caliber retinal arteries	No digitalis given before electrocardiogram; inverted T-wave in Leads I-II
157	16 F	Mitral stenosis; obliterative pericarditis	108	58	None	505	180	Mitral stenosis	Obliterative fibrous pericarditis	0	0	Renal lesions negative	No digitalis given; inverted T-wave in Leads II-III

TABLE XVI

CASES OF ADHERENT PERICARDIUM

CASE	AGE AND SEX	AVERAGE BLOOD PRESSURE		VENTRICULAR PREPONDERANCE	WEIGHT OF HEART, GM.		VALVES	PERICARDIUM	CORONARY SCLEROSIS		CEREBRAL VESSELS	MISCELLANEOUS
		SYSTOLIC	DIASTOLIC		AT NECROPSY	ESTIMATED NORMAL			RIGHT	LEFT		
3	66 F	130	80	None	With pericardium, 495		Slight thickening of mitral valve; no stenosis	Cannot be separated from heart	1+	1+	Cerebral embolism; infarction in brain	No digitalis given; inverted T-wave in Leads I-II-III; auricular fibrillation; right auricle dilated 3+; no infarction
28	22 M	102	68	None			Moderate fibrous thickening of tricuspid, mitral, and aortic	Marked fibrous completely obliterative pericarditis	0	0		No digitalis given; inverted T-wave in Leads I-II-III; ascites; serofibrinous peritonitis; obliterative pleuritis and pericarditis (Pick's disease)
64	57 M	120	75	Left	675	353	Negative	Complete obliteration of pericardium	1+	1+		Six c.c. of digitalis before first electrocardiogram; fourteen c.c. before second; inverted T-wave in Leads I-II of second electrocardiogram; enormous hypertrophy of left ventricle
84	27 F	108	62	None			Negative	Heart fastened to base of pericardium by tumor mass	0	0		No digitalis given; inverted T-wave in Leads I-II; inferior surface of heart invaded by tumor mass
98	26 F	115	90	None	273	180	Negative	Complete obliteration of pericardium	0	0		No digitalis given; inverted T-wave in Leads II-III; small infarction in thickened pericardium on posterior surface of left ventricle but not involving myocardium

Leads I and II. In three cases the T-waves were inverted in Leads II and III. In two of the cases in the latter group conditions producing strain predominantly on the left ventricle were present, but the tendency of this to modify the type of changes in the T-wave was overbalanced by the effect of infarction in the posterior portion of the left ventricle. In one case in which the T-waves were inverted in all leads, chronic diffuse fibrosis in the anterior portion of the left ventricle existed.

Miscellaneous Cardiac Diseases.—A miscellaneous group of sixteen cases, difficult to classify because of multiple factors productive of myocardial strain, was studied (Table XV). A definite analysis of these cases in relation to strain exerted predominantly on one of the ventricles is not possible.

Chronic Adherent Pericarditis.—Five patients with chronic adherent pericarditis were studied (Table XVI). As pointed out before, it is impossible to say whether this condition exerts a strain predominantly on one or the other ventricle. The average age of the patients in this group was thirty-nine and six-tenths years. The average blood pressure was 110 mm. systolic and 75 mm. diastolic. The average cardiac weight was 481 gm., which exceeded the calculated average normal cardiac weight by 266 gm. In two cases there was inversion of the T-waves in Leads I, II, and III. In two cases the T-waves were inverted in Leads I and II, and in one of these sufficient digitalis had been administered before the tracing was obtained to lay its value open to question. In one case the T-waves were inverted in Leads II and III. Ventricular preponderance was present in only one case, a fact worthy of note although its meaning is not clear. These cases did not lend themselves to analysis on the basis of differential ventricular strain.

GENERAL COMMENT

From a consideration of 117 cases (Table XVII) of cardiac lesions which throw a definite or probable strain preponderantly on the left ventricle, it is seen that in 83.7 per cent of them there were inverted T-waves in Lead I or in Leads I and II in the electrocardiogram. In nine cases (7 per cent), there was inversion of the T-waves in Leads II and III. In seven of these cases there was myocardial infarction in the posterior portion of the left ventricle which accounted for the inversion of the T-waves in Leads II and III. In eleven cases (9.4 per cent), the T-waves were inverted in all leads. Certain of these cases may include those in which the inversion of the T-waves in Lead III is not of abnormal significance, and such cases would fall in the group with inversions of the T-wave in Leads I and II. Thus, when strain predominantly on the left ventricle produces inversion of the T-wave, the inversion is found in Lead I or in Leads I and II in a high percentage of cases.

In Table XVII six cases are recorded in which there were lesions which would throw strain predominantly on the right ventricle. In 83.3 per cent of these cases, the T-waves were inverted in Leads II and III and in no instance did there occur inversions of the T-wave in Lead I or in Leads I and II. In one case, the T-wave was diphasic in all leads. Here the association of inverted waves in Leads II and III with conditions which produce right ventricular strain is striking. The number of cases in this group is so small that in order to establish inversions of the T-wave in Leads II and III, as an expression of strain preponder-

TABLE XVII

DISEASES CAPABLE OF PRODUCING VENTRICULAR STRAIN

	DISEASE	CASES	HEART WEIGHT, GM.	EXCESS OF ESTIMATED NORMAL WEIGHT, GM.	LEFT VENTRICULAR STRAIN PER CENT: INVERTED T IN LEADS I OR I-II	PER CENT: INVERTED T IN LEADS II-III	PER CENT: INVERTED T IN LEADS I-II-III	CASES: INVERTED T IN LEADS I OR I-II	CASES: INVERTED T IN LEADS II-III	CASES: INVERTED T IN LEADS I-II-III
1	Definite hypertension	42	604	280	90.5	4.7	4.7	38.0	2	2
2	Probable hypertension	13	607	258	100.0			13.0		
3	Definite hypertension and marked coronary sclerosis	9	584	252	88.8		11.2	8.0		1
4	Probable hypertension and marked coronary sclerosis	6	478	221	83.3		16.6	5.0		1
5	Syphilitic aortic insufficiency	8	620	313	75.0		25.0	6.0		2
6	Rheumatic aortic endocarditis	7	569	290	71.4		28.6	5.0		2
11	Myocardial infarction and definite hypertension	21	579	252	71.4	19.0	9.5	15.0	4	2
12	Myocardial infarction and probable hypertension	11	537	209	63.6	27.2	10.0	7.0	3	1
	Total	117			83.7	7.0	9.4	97.0	9	11
	Right Ventricular Strain									
9	Mitral stenosis	3	536	232		66.6	33.3		2	1
9	Mitral insufficiency	1	385	43		100.0			1	
9	Chronic pulmonary disease	2				100.0			2	
	Total	6				83.3	16.6		5	1
	Right and Left Ventricular Strain									
7	Mitral stenosis and aortic stenosis and insufficiency	7	498	199	14.3	85.7		1.0	6	
7	Aortic and mitral endocarditis	1	478	115			100.0			1
8	Hypertension and mitral stenosis	2	589	249		50.0	50.0		1	1
8	Hypertension and mitral endocarditis with stenosis	2	555	305	66.6	33.3		2.0		
	Total	12			22.8	62.0	15.2	3.0	7	2

antly of the right ventricle, the collection of further cases yielding the same result will be required.

There were twelve patients (Table XVII) with a combination of diseases, such that strain could be exerted on both ventricles. The strain on the right ventricle in all of these cases was produced by mitral endocarditis with or without stenosis. The T-waves were inverted in Leads II and III in seven of twelve cases (62 per cent). In three cases (22.8 per cent) the T-waves were inverted in Lead I or in Leads I and II. The incidence of inversion of the T-waves in Leads I and II (22.8 per cent as compared with 83.7 per cent) is much lower in diseases producing strain predominantly on the left ventricle when mitral endocarditis is associated than when it is absent. It has been suggested previously, in a discussion of the combined group of mitral stenosis, aortic stenosis and insufficiency, that when the two conditions compete in producing strain predominantly on the right or the left ventricle respectively, disease of the mitral valve may place a more serious strain on the right ventricle than that which aortic disease places on the left ventricle. If this assumption is correct, it is possible that a similar condition results at times in combinations of hypertension and mitral stenosis and that the predominant inversion of the T-waves in Leads II and III, shown in this group, is an expression of strain predominantly on the right ventricle, due to mitral valvular disease.

We have been unable to make any definite correlation between cardiac weight and the type of changes in the T-wave that occurred. For example, the average cardiac weight, and its excess over the calculated normal weight, was found to be essentially the same in definite or probable hypertension, associated with coronary sclerosis and without infarction, as that in the groups of mitral stenosis and mitral and aortic stenosis. Yet in the group with hypertension and coronary sclerosis the inversion of the T-waves is chiefly in Lead I or in Leads I and II and in the groups with mitral stenosis and with mitral and aortic stenosis, chiefly in Leads II and III. That large hearts give a high percentage of inversions of the T-wave in Lead I or in Leads I and II is explained by the fact that the conditions which produce the largest hearts are those conditions which produce a clear-cut strain on the left ventricle.

Attention has been directed to the fact that there were only two cases of coronary sclerosis unassociated with either definite or probable preexistent hypertension, or with myocardial infarction, in which significant inversions of the T-wave occurred. This seems to indicate that some additional factor, such as hypertension or myocardial infarction, is necessary in cases of coronary sclerosis to produce inversion of the T-wave. This seems a reasonable explanation of the fact, observed by

Willius[27] and others, that in many cases of angina pectoris there are no significant changes in the T-wave.

It must not be forgotten, furthermore, that inversions of the T-wave following infarction tend to disappear in from six months to two years, provided the patient survives.[19, 21, 24] Therefore, discovery of inversions of the T-waves in these cases will depend on the time the electrocardiogram is taken in relation to the time of infarction.

Fifty-two patients with myocardial infarction, either with or without hypertension, are included in this study. This number constitutes nearly 30 per cent of the total group and emphasizes the frequency with which myocardial infarction is found in patients who exhibit significant changes in the T-wave. The evidence at hand indicates that infarction is a more dominant factor than differential ventricular strain in determining the type of inversion of the T-wave produced. Further, infarction of the anterior portion of the left ventricle and septum (the region supplied by the left coronary artery) produces inversion of the T-wave in Lead I, or in Leads I and II, whereas infarction of the posterior portion of the left ventricle and septum (the region usually supplied by the right coronary artery) causes inversion of the T-wave in Leads II and III. These cases will be discussed in detail elsewhere.[2]

Numerous reports have appeared in the literature regarding the effect of administration of digitalis on the electrocardiogram. The recent observations of Bromer and Blumgart indicate that the earliest effect of digitalis is to change the amplitude of the T-wave in all leads. This phenomenon was observed by Cohn, Fraser, and Jamieson. Following this, Bromer and Blumgart observed that the R-T or S-T interval in Lead III became depressed, less elevated, or altered in general shape. The more pronounced effects which they obtained with greater dosage consisted of further alterations in the R-T or S-T interval, and they noted that the greatest change occurred in Lead III, slightly less in Lead II and least of all in Lead I. Pardee[26] has noted this peculiar modification of the S-T interval and has illustrated it by figures in his text. There is a distinct tendency exhibited in his tracings for the T-waves to become diphasic as a result of the modification of the S-T interval. Kerr, in discussing a paper by Berman and Mason, stated that he had noted development of an inverted T-wave in Lead III more frequently than in Leads I and II following treatment with digitalis. We have observed the peculiar depression of the R-T interval in our tracings following administration of digitalis and particularly in Leads II and III. At times, the T-waves are actually inverted in those leads. Obviously the effect of administration of digitalis on changes in the T-wave is highly important in the analysis of cases such as those presented in this study.

THEORETIC CONSIDERATION

The facts presented in this paper warrant considerable discussion in relation to the mechanism of production of inversion of the T-wave. The facts are oriented best when considered in the light of the evidence presented by Wilson and Herrmann that the T-wave of the normal ventricular complex is a combination of right and left ventricular effects. Lewis[15] interprets their study to mean that "In Lead III and usually in Lead II the end phase of the dextrocardiogram would be directed downward and in the levocardiogram it would be the reverse." In that case the upright T-wave of the normal electrocardiogram would be attributable to a preponderance of the right ventricular effect in Lead I and of left ventricular effects in Leads II and III. In a consideration of events in the formation of the T-wave in bundle-branch block, Wilson and Herrmann call attention to the fact that the upstroke of the T-wave in right bundle-branch block is due chiefly to the early decline of the process of excitation in the left ventricle. However, they admit that it may be due to preponderant right ventricular effects in the form of preponderance of retained activity on the right side of the heart. They stated that there is as much basis for the latter view as for the former.

It is necessary to consider conditions present in the individual fractionate components of cardiac muscle in normal or abnormal states to understand factors which determine changes in the T-wave. It seems justifiable to consider that ventricular strain results in a disturbed physiological status of the fiber, best described as a state of fatigue. The most important factor in fatigue in muscle has been shown to be the hydrogen-ion concentration.[1, 8, 11, 23] The conduction time and excitability of the cell are decreased by an increase in the hydrogen-ion concentration.[1, 8] Fulton stated that in fatigue some fibers are more affected than others (leading to asynchronism). Mines stated that a slight increase in hydrogen-ion concentration diminishes the duration of the electrical change in cardiac muscle. Redfield and Edsall studied the effect of fatigue in the ventricle of the tortoise, in an oxygen-free atmosphere, and found that the amplitude of contraction decreased logarithmically to the point of extinction, that the amount of lactic acid increased step by step with the degree of fatigue, and that the duration of contraction does not increase in cardiac muscle as it does in skeletal muscle when fatigued. The results summarized here indicate that fatigue or increased hydrogen-ion concentration diminishes amplitude of contraction, duration of electrical effect, conductivity, and excitability in cardiac muscle. It seems reasonable to expect these changes to be manifest predominantly in the ventricle that is subject to the greatest strain.

Katz and Weinman consider that the T-wave is the result of asynchronous cessation of electrical activity in the fractionate components of heart muscle. They consider that differences in initial tension and arterial resistance in the two ventricles and variable nutrition in different regions of the ventricles are factors capable of producing variation in the duration of fractionate contractions. If the conclusion of Wilson and Herrmann is accepted, that the T-wave is a combination of right and left ventricular effects, then three main possibilities may be considered as to the cause of inversion of the T-wave in Leads I and II in left ventricular strain, with its consequent disturbance of the physiological status of the muscle fiber. First, there may be a disturbance in electropotential balance, due to diminished duration of the electrical change in many or in all of the fractionate components of the left ventricle; second, the disturbance in electropotential balance may be due to early decline of the process of excitation in certain or in all of the fractionate components; third, the preponderance of retained activity in the relatively normal right ventricle may be the factor determining the inversion of the T-wave in these leads. In right ventricular strain, on the other hand, with inverted T-waves in Leads II and III, the first two of these three factors may be conceived as acting in the right rather than in the left ventricle; and the third factor may be exerted in the left rather than in the right ventricle. This consideration is based on the supposition that a plane exists in the heart about which the right and left ventricles act as opposing forces in their effect on the T-wave. That this plane is one accurately separating the right and left ventricles seems questionable on the basis of some observations we have made in infarction of the left ventricle.

We have called attention to our observation that infarction of the anterior portion of the left ventricle and apex is associated with inversion of the T-wave in Leads I and II, whereas infarction in the posterior surface of the left ventricle and posterior one-third of the septum in the region usually supplied by the right coronary artery produces inversion of the T-wave in Leads II and III. In other words, the infarction in the latter region produces the same changes in the T-wave as those encountered in strain of the right ventricle. This similarity in effect suggests that the posterior part of the left ventricle and septum may act with the right ventricle to produce an electrical change opposed in the direction of its action on the T-wave to that produced by the anterior two-thirds of the left ventricle and septum and that the resultant of these forces determines the direction of the T-wave. If this observation is valid, then the plane separating the electrical forces which exert an influence on the T-wave divides the left ventricle in such a way that the posterior part of the left ventricle and posterior one-third of the septum act with the right ventricle. This may be one reason why strain on the right ventricle infrequently produces inver-

sion of the T-wave; the muscular mass of the right side of the heart is relatively small in comparison with the anterior two-thirds of the left ventricle and septum. Wilson and Herrmann attempted to explain how the thin-walled right ventricle at times can produce effects of greater amplitude on the T-wave than the thick-walled left ventricle. This fact would be rendered much more comprehensible if it is true, as it appears to be, that a portion of the left ventricle acts in conjunction with the right ventricle in producing electrical effects relating to the form and direction of the T-wave.

The possibility must be borne in mind that preponderant hypertrophy of the left or of the right ventricle plays an important rôle in determining the changes in the T-wave seen in differential ventricular strain. It is true that preponderant hypertrophy of one verticle bears

TABLE XVIII

VENTRICULAR PREPONDERANCE IN THE CASES STUDIED

DISEASES	CASES	PREPONDERANCE WITH INVERTED T-WAVE IN LEADS I-II			PREPONDERANCE WITH INVERTED T-WAVE IN LEADS II-III			PREPONDERANCE WITH INVERTED T-WAVE IN LEADS I-II-III		
		RIGHT	LEFT	NO PREPONDERANCE	RIGHT	LEFT	NO PREPONDERANCE	RIGHT	LEFT	NO PREPONDERANCE
Definite hypertension	37	1	26	6	1	1	0	0	0	2
Probable hypertension	11	1	9	1	0	0	0	0	0	0
Definite hypertension and definite coronary sclerosis	9	0	7	0	0	0	0	0	1	1
Probable hypertension and definite coronary sclerosis	6	0	4	1	0	0	0	0	1	0
Syphilitic aortic insufficiency	8	0	5	1	0	0	0	0	1	1
Aortic stenosis and insufficiency	7	0	4	1	0	0	0	0	0	2
Aortic insufficiency and mitral stenosis	8	0	0	1	3	2	1	0	1	0
Hypertension and mitral stenosis	5	0	2	1	0	0	1	1	0	0
Strain on right side of heart	6	0	0	0	4	0	2	0	0	0
Coronary sclerosis	1	0	0	0	0	0	0	0	0	0
Myocardial infarction with definite hypertension	20	1	10	4	2	0	1	0	1	1
Myocardial infarction with probable hypertension	7	1	5	0	0	0	1	0	0	0
Myocardial infarction	11	0	4	2	1	2	2	0	0	0
Myocardial infarction with miscellaneous diseases	6	0	2	1	1	1	0	0	0	1
Miscellaneous diseases	14	1	3	2	4	1	2	0	1	0
Adherent pericardium	5	0	1	1	0	0	1	0	0	2
Total	161	5	82	22	16	7	11	1	6	11

a fairly constant relationship to strain predominantly of that ventricle. It is possible that this hypertrophy may modify the period of activation or the electrical potential available for an effect on the T-wave and thus disturb the normal electrical balance between the two ventricles.

The factors producing preponderance in the electrocardiogram can be correlated only roughly with the type of inversion of the T-wave (Table XVIII). In general, inversion of the T-waves in Lead I or in Leads I and II is attended by a high incidence of left ventricular preponderance, whereas there is a fairly high incidence of right ventricular preponderance when the T-waves are inverted in Leads II and III. There was no evidence of preponderant influence of one ventricle in the electrocardiogram in one-fifth of the patients who exhibited inversion of the T-wave in Lead I or in Leads I and II, and one-third of the patients in whom inversions of the T-wave occurred in Leads II and III gave no evidence of preponderance of one ventricle. In nearly two-thirds of the patients with simultaneous inversions of the T-wave in all leads of the electrocardiogram, there was no evidence of ventricular preponderance. It seems evident that the factors that determine ventricular preponderance are not the same as those responsible for types of inversions of the T-wave. We cannot deny the probability that there may be some factors in common in the two processes.

It is well recognized that patients die from strain predominantly of the right or of the left ventricle, without ever showing significant inversions of the T-wave in the electrocardiograms. The studies of Willius[27, 31] have shown that in cases in which the heart was subjected to strain predominantly on one side, and in which there were inversions of the T-wave, the prognosis was much worse than in cases in which there were comparable lesions but in which significant inversion of the T-wave did not occur. The question naturally arises as to what determines the time at which changes in the T-wave make their appearance in conditions of prolonged ventricular strain as observed, for example, in hypertension or in aortic insufficiency. The most logical answer to this seems to be that it is a question of the degree to which overwork and fatigue interfere with the normal physiological activity in the muscle cells. It must be true, as in other tissues in the body, that a wide range of physiological adjustment or compensation can take place in heart muscle which is subjected to fatigue or to overstrain. However, it is probable that when fatigue or strain reaches or exceeds a certain limit, uncompensated metabolic disturbances occur, capable of modifying the electrical forces produced by the right and left portions of the heart and thus to bring about significant inversions of the T-wave. If these assumptions are correct, a rational basis is furnished for the poor prognostic outlook of patients in whose electrocardiograms significant inversions of the T-wave occur.

Finally, it should be mentioned that Daly, in experiments on dogs, in which he was able to place varying work loads on the two ventricles, found that, when the left ventricle performs excessive work, increased positivity of the T-wave in Lead III, and increased inversion of the T-wave in Lead I resulted. In two of Daly's experiments, performed on animals in which the T-wave in Lead III was inverted, the pulmonary artery was partly occluded by a clamp. In one of these experiments, application of the clamp caused an increase in the amplitude of the inverted T-wave. These results are in accord with changes in the T-wave observed in this study in relation to strain predominantly of the right and of the left sides of the heart. Furthermore, Otto has observed that in axial leads in the dog sudden increased work imposed on the right ventricle produced temporary inversion of the T-wave, while a sudden increase in the work imposed on the left ventricle tended to produce the opposite effect on the T-wave.

DIAGNOSTIC INDICATION OF INVERSION OF THE T-WAVE

If our interpretations of the facts presented in this paper are correct, then an inverted T-wave in Lead I or in Leads I and II is indicative of a lesion throwing strain predominantly on the left ventricle, whereas an inverted T-wave in Leads II and III indicates a lesion throwing a strain predominantly on the right ventricle. If conditions recognized as throwing a definite strain on the left ventricle, such as aortic stenosis or hypertension, show an inverted T-wave in derivations II and III, then we are led to suspect that, in addition, some lesion is present causing overload of the right ventricle or that infarction has occurred in the posterior portion of the left ventricle.

SUMMARY AND CONCLUSIONS

1. One hundred seventy-seven cases in which there were significant changes in the T-wave, and in which necropsy was performed, have been studied for evidence of relation between differential ventricular strain and the type of changes in the T-wave.

2. In cases in which the strain was thrown predominantly on the left ventricle, there was inversion of the T-waves in Lead I or in Leads I and II (84 per cent) and in only 7 per cent were the T-waves inverted in Leads II and III. Infarction was found in the posterior surface of the left ventricle in all but two cases in which electrocardiograms showed inversion of the T-waves in Leads II and III.

3. In cases in which the condition produced disproportionate load on the right ventricle, T-waves were inverted in Leads II and III in 83 per cent and no case showed inversion of the T-wave in Lead I or in Leads I and II.

4. In conditions in which multiple lesions compete for maximal strain on the two ventricles, the leads in which the T-waves will be

inverted cannot be predicted. It seems likely that the type of inversion of the T-wave encountered may be related to the ventricle suffering the greater stress in accordance with the two previous observations.

5. This differential effect of right or left ventricular strain on the type of inversion of the T-wave is in partial accord with the conclusion of Wilson and Herrmann that the T-wave of the normal ventricular complex is a combination of right and left ventricluar effects. The inversions encountered here are considered to be due to interference with the normal summation of right and left ventricular effects, that in turn are due to a disturbance of physiological conditions and electrical effects in the ventricle subjected to excessive strain.

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THE ELECTROCARDIOGRAM IN PERICARDIAL EFFUSION*

I. Clinical

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FOUR years ago one of us (R. W. S.) observed a patient with the typical signs of acute pericardial effusion whose electrocardiogram exhibited the monophasic R-T deviation characteristic of recent myocardial infarction. The curves were indeed so typical that the clinical diagnosis of coronary thrombosis and myocardial infarction was submitted. Much to our surprise the post-mortem examination revealed no significant changes either in the myocardium or in the coronary arteries, but a hemorrhagic effusion into the pericardial sac from a ruptured aneurysm of the ascending aorta. More recently we have seen an additional case of acute pericardial effusion with similar, although not such marked, changes in the electrocardiogram. These clinical observations appeared of sufficient importance to merit further study of the question in experiments on animals. The details of the experimental observations are presented in the paper following this one, but it may be stated here that acute pericardial effusion in dogs produced changes in the electrocardiogram similar to those observed in man.

CASE REPORT

A colored male, G. H., 53 years old, a laborer, was admitted November 9, 1925, complaining of breathlessness and attacks of substernal pain. He had had a primary luetic infection 27 years previously, otherwise he had enjoyed good health. The patient stated that he had been able to do manual labor until the onset of his present trouble one month before. This had begun with paroxysmal attacks of substernal pain, radiating to the neck, and later breathlessness on exertion appeared. However, he had not been bedridden until two days before admission when he was seized with a severe substernal pain and great respiratory distress.

Physical Examination.—This revealed a well-developed, colored male in acute distress from orthopnea. The pupils were small, unequal, and reacted in accommodation but not to light. There was no visible precordial activity. The area of cardiac dullness extended to the mid-axillary line in the fifth and sixth intercostal spaces, and 2 cm. to the right of the sternum in the third and fourth intercostal spaces. The heart sounds were quite muffled, but no adventitious sounds were audible. Palpation of the larger accessible arteries showed a marked diminution in pulse volume with the typical pulsus paradoxus. The blood pressure was 110 mm. Hg. systolic and 80 mm. Hg. diastolic. The signs of compression were elicited over the left lung base posteriorly. The breath sounds were accentuated throughout, but there was no demonstrable moisture at the lung bases. The liver extended almost to the umbilicus in the midline but was not tender, and there

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was no edema over the sacrum or the lower extremities. The patellar and Achilles tendon reflexes were absent on both sides. The blood Wassermann was four plus. The spinal fluid showed an increased globulin content, 150 small mononuclear cells per cubic millimeter and a four plus Wassermann reaction. Fluoroscopically,

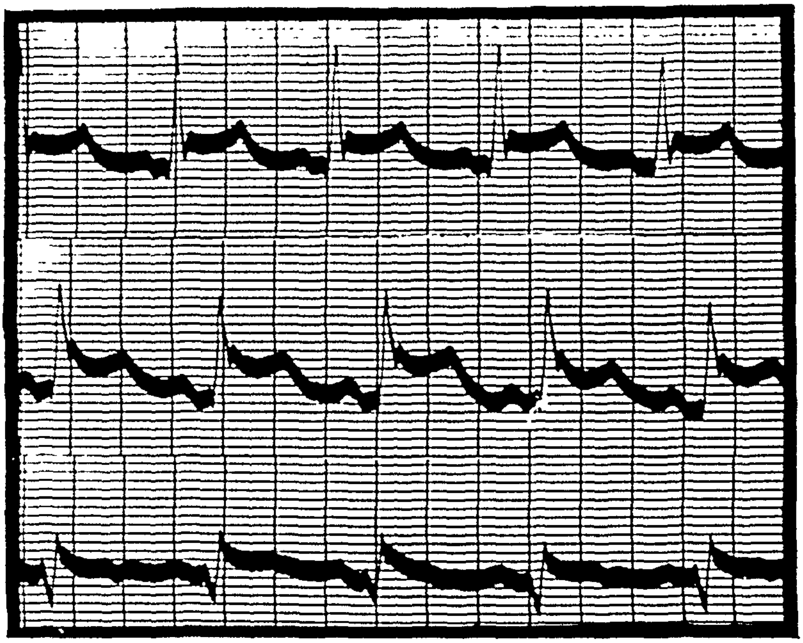

Fig. 1.—Three leads in a case of hemopericardium from a ruptured aneurysm. Note the abnormal ventricular complexes; the positive R-T deviation in Leads I and II, and the S-T segment above the iso-electric level in Lead III. In this figure and those following, the vertical lines represent 0.2 sec.; the horizontal lines 0.1 millivolt.

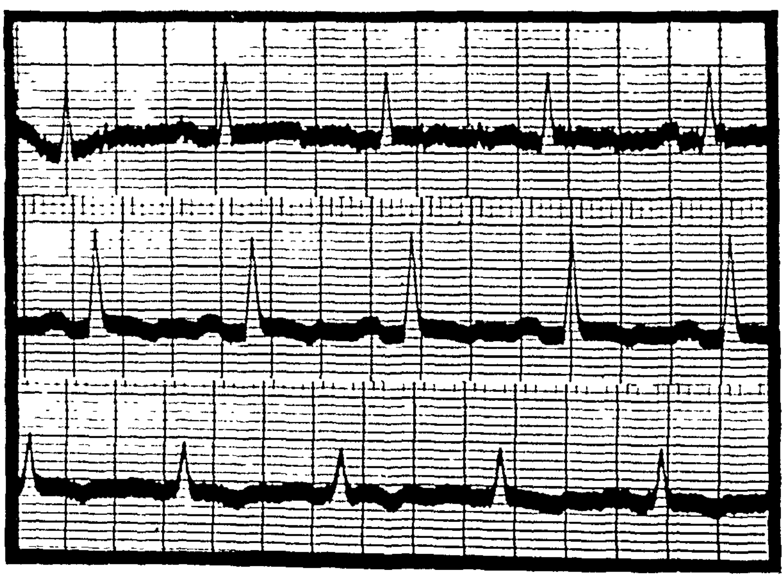

Fig. 2.—From the same patient thirty-three days after Fig. 1, and one week before death. Note the change in the ventricular complexes.

in the anteriorposterior view a marked increase was observed in the transverse diameter of the heart shadow to the right and to the left, and also an increase in the width of the great vessels. There was no appreciable movement of the heart with respiration, and the cardiac pulsations were very feeble. Projecting

into the lung field from the region of the right auricle there was a tumor mass the size of a billiard ball which did not pulsate. On rotating the patient this mass appeared to be posterior to the ascending aorta but did not infiltrate the lung field.

Clinical Course.—Since the clinical picture and fluoroscopic findings in this patient suggested pericardial effusion; the day following admission, a paracentesis of the pericardium was attempted, and 5 c.c. of blood were withdrawn, but it was thought at the time that this came from within the heart. A day later the electrocardiogram shown in Fig. 1 was obtained. This record was regarded as reliable evidence of recent myocardial infarction, and accordingly the patient throughout the remainder of his stay in the hospital was treated as a case of coronary thrombosis. He continued to have a low grade fever but never above 38° C. Dyspnea became more marked, the pulse volume diminished, edema of the lower extremities appeared, and the patient died November 20, 1925, forty-two days after admission. Seven days *before* his death the electrocardiogram shown in Fig. 2 was obtained. The following clinical diagnosis was submitted: Coronary arteriosclerosis with occlusion; myocardial infarction; cardiac hypertrophy and dilatation; syphilitic aortitis; aneurysm of the ascending aorta; cerebrospinal syphilis.

Autopsy Findings.—The heart, pericardium and aorta were removed *en masse*. On opening the pericardium 200 c.c. of hemorrhagic fluid escaped. Both the visceral and parietal layers were thickened, in some areas as much as 3 mm. The surfaces were markedly blood tinged, irregular and covered by a bloody, partially organized exudate. Throughout the pericardial cavity there were numerous bands of adhesions, some measuring 3 mm. in diameter. On cut section of both the visceral and parietal pericardium the deeper portions were edematous and showed marked vascularization. The heart was flabby and dilated but contained no antemortem thrombi. The mural endocardium and cardiac valves showed no evidence of disease. The columnae carneae and papillary muscles were enlarged and flattened, particularly on the right side. Several cut sections of the myocardium showed no gross areas of fibrosis or infarction. The coronary arteries were not narrowed at their mouths and when opened showed only moderate intimal changes. No thrombosis or reduction in lumen was found. The aorta was markedly dilated and inelastic throughout the ascending portion, the arch, and in the first few centimeters of the thoracic descending portion. The intima was thickened and corrugated and presented the typical gross appearance of syphilitic aortitis. Four centimeters proximal to the orifice of the innominate artery there was a circular opening in the aortic wall 3 cm. in diameter leading to a small aneurysmal sac 5 cm. in diameter, which was filled with a mottled, friable thrombus. On removing this thrombus one saw in the bottom of the sac a rupture 12 mm. in diameter which connected directly with a cavity in the visceral pericardium containing 175 c.c. of recent blood clot. The wall of this cavity contained an organized exudate which in some areas was elevated by recent hemorrhage.

Anatomical Diagnosis.—Syphilitic aortitis; saccular aneurysm of the ascending aorta with rupture into the pericardium; hemopericardium; organized pericarditis; chronic passive congestion of viscera; moderate hypertrophy and dilatation of the heart.

DISCUSSION

The clinical course in the above case may be interpreted in the light of the autopsy findings as follows: The long-standing syphilitic process in the aorta led to characteristic changes in the vessel wall with the formation of an aneurysmal sac opening 4 cm. proximal to the innomi-

nate artery. The process, however, spared the aortic ring, the valve leaflets, and the mouths of the coronary arteries, so that the heart was not embarrassed, and, as one frequently observes in such cases, the patient was able to work at manual labor until two months before death. His first symptoms—attacks of substernal pain and dyspnea—continued for three weeks, at which time he had an acute attack of substernal pain accompanied by great respiratory distress which incapacitated him and for which he sought admission to the hospital. It seems likely that this attack occurred at the time of rupture of the aneurysm into the pericardial sac; more certain is it that the clinical picture observed on admission was due to hemopericardium. As stated above, our initial impression of the case was pericardial effusion, hence an exploratory paracentesis was done, but not suspecting hemopericardium, the blood obtained from the puncture was thought to have come from the heart cavity. The day following, the electrocardiogram (Fig. 1) was obtained. This appeared to afford indisputable evidence of a recent cardiac infarct, and our original diagnosis of pericardial effusion was disregarded. The attack of substernal pain and dyspnea two days before admission was now ascribed to coronary thrombosis, and the clinical course of progressive circulatory failure was explained on the basis of myocardial infarction.

Referring now to the electrocardiogram, Fig. 1, it is clear that these curves display the positive S-T deviation seen in recent myocardial necrosis. They are typical with one exception; the S-T segment is above the iso-electric level in all leads, whereas in clinical curves the S-T segment is usually oppositely directed in Leads I and III, thus an S-T elevation in Lead I is accompanied by an S-T depression in Lead III and vice versa.

That characteristic abnormalities in the R-T segment of the electrocardiogram are associated with myocardial necrosis is a fact well established on both experimental[1, 2, 3, 4, 5, 6] and clinical[7, 8, 9, 10, 11, 12, 13, 14] grounds, and need not be discussed here; but so far as we are aware, there has appeared no evidence to show that effusion into the pericardial sac per se causes a deformity of the S-T segment similar to that seen in recent myocardial infarction. With the exception of coronary occlusion, and in moribund states, the only clinical curves showing similar R-T deviations are those obtained from patients with rheumatic carditis, and it is generally assumed that the deviation is due to the rheumatic myocardial lesion. In their paper on "Electrocardiographic Evidence of Myocardial Involvement in Rheumatic Fever," Cohn and Swift[13] present two curves from patients showing a positive R-T deviation, but one cannot ascertain from reading their paper whether or not these patients had a complicating pericardial effusion. Recently Porte and Pardee[14] reported three cases of rheumatic pericarditis with curves showing a slight upward convexity of the S-T segment preceding a

negative T-wave—the so-called coronary T-wave. The authors ascribed these changes to the rheumatic myocardial lesions and state: "We believe that the T-wave abnormality observed in these three cases of pericarditis is due to a complicating myocardial inflammatory reaction." Although Porte and Pardee[14] entitle their paper: "Coronary T-wave in Rheumatic Pericarditis," no significance is attached to the pericardial lesion or to the effusion in the pericardial sac in spite of the fact that the pathological report in their one autopsied case reads: "The pericardium contains an excess of hemorrhagic fluid."

Considerable difficulty is frequently encountered in determining the significance of myocardial lesions in electrocardiographic abnormalities. The above case of hemopericardium with no complicating myocardial lesion is a particularly good clinical illustration of the effect of hydrostatic pressure in the pericardial sac on R-T deformities in the electrocardiogram. We have observed other clinical cases in which the evidence was suggestive but not so conclusive, and we therefore hesitate to present them as clear-cut examples. Two, however, are sufficiently instructive to merit a brief discussion.

The first of these was a case of pyopericardium in a white male, aged 56 years, who was seen by one of us (H. S. F.) six days after the onset of an acute illness which began with a chill, fever, and later pain in the left chest. He had the physical signs of effusion over the left lower lobe, and the initial diagnosis was empyema complicating pneumonia. Pus was aspirated from the left chest. Seven days after admittance to the hospital, and thirteen days after the onset of this illness, the electrocardiogram reproduced in Fig. 3 was obtained. The positive S-T segment in Leads I and II suggested a coronary lesion with myocardial infarction. Eight days later, and twelve hours before death, the record in Fig. 4 was made, which displays a more normal appearance. At the post-mortem examination the pericardium contained 400 c.c. of a thick, viscid pus similar to that found in the left pleural cavity. No thrombi or narrowing of the coronary arteries were observed and the endocardium, the heart valves, and myocardium showed no gross changes. Histologically, sections of the myocardium showed obscure striations of the muscle fibers, which were larger than normal in some areas. Some fragmentation and segmentation of the muscle fibers was also observed. The epicardium was markedly thickened, measuring from 4 to 6 mm. in width. In the superficial layers there was an abundant fibrin deposit with a moderate number of round cells, mononuclears and polymorphonuclears. In the deeper layers there was organization of the exudate with numerous fibroblasts, and a moderate round cell infiltration. A section stained by Gram's method showed a few gram positive lancet-shaped diplococci (pneumococci) in the exudate.

The above case of purulent pericarditis with effusion affords suggestive but not conclusive evidence, since there remains the question of the possible effect of the myocardial damage associated with infection. At all events, this observation proves that the R-T deviation cannot be accepted as indisputable evidence of myocardial infarction, and further points to the value of such deviations in the early diagnosis of effusion in the pericardial sac.

Another case exhibiting R-T abnormalities was one of rheumatic carditis in a colored boy, 16 years old, who was seen two weeks after the onset of a typical attack of acute rheumatic fever with multiple migratory arthritis. When first observed, the patient was acutely ill with fever, dyspnea and orthopnea. The area of cardiac dullness was definitely increased both to the right and to the left

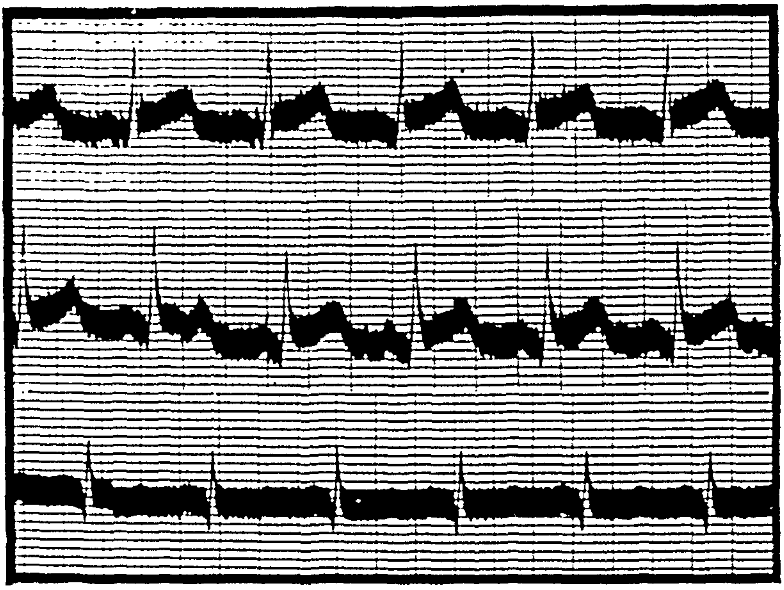

Fig. 3.—Three leads from a case of purulent pericarditis with effusion. Note the high take-off of the S-T segment in Leads I and II which merges with the T-wave.

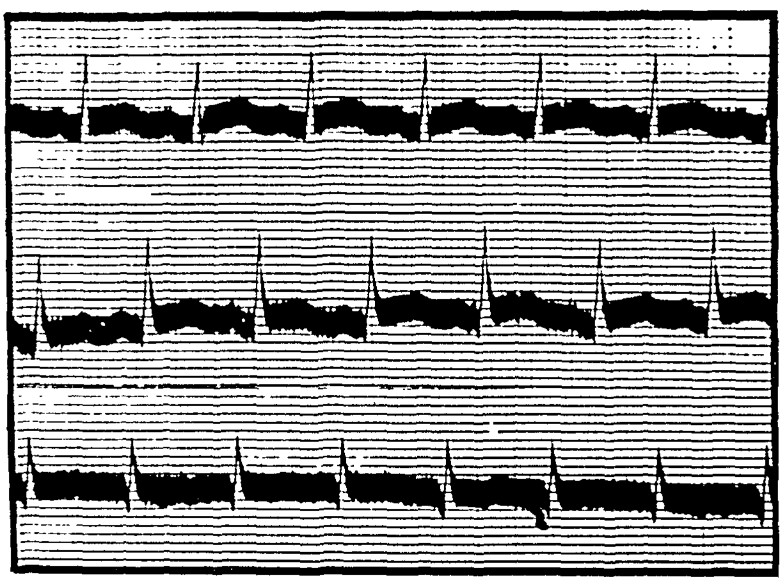

Fig. 4.—From the same patient eight days after Fig. 3, and twelve hours before death. Note the approach of the S-T segment and T-wave toward the iso-electric level.

(verified by x-ray), the heart sounds were muffled, signs of compression were elicited over the left base posteriorly, and a friction rub was audible over the precordium. At this time the record shown in Fig. 5 was made, and nineteen days later when the patient was much improved clinically, the record in Fig. 6 was obtained. Pericardial effusion was suspected in this case but never proved, hence we cannot

conclude that the R-T deviation in Fig. 5 was caused by pericardial effusion. However, since this possibility existed, the conclusion that the rheumatic myocardial lesion caused the R-T deviation is not acceptable without further proof.

We are not contending here that rheumatic myocardial lesions may not also cause deformities in the ventricular complex of the electro-

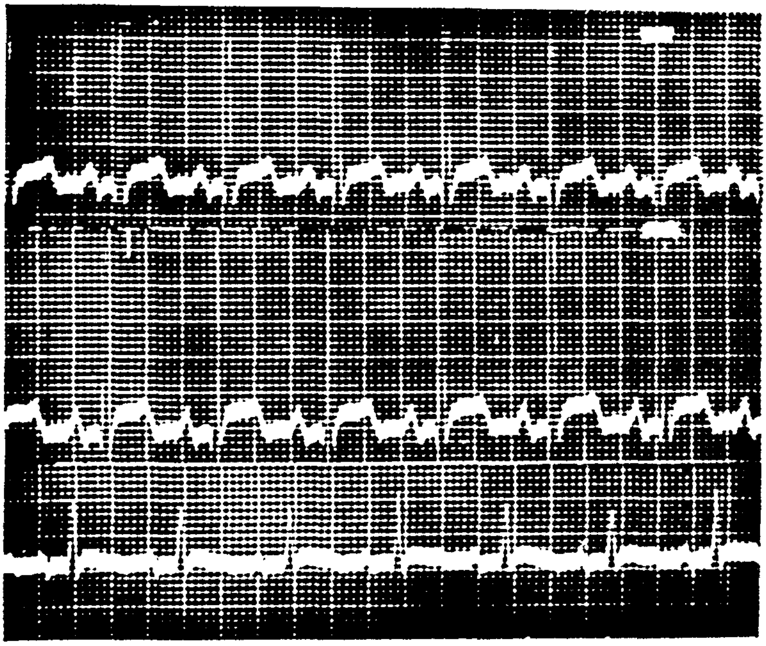

Fig. 5.—Curves from a case of rheumatic carditis, suspected of having a pericardial effusion. Note that the S-T segment is distinctly elevated above the isoelectric line and merges with an upright T-wave.

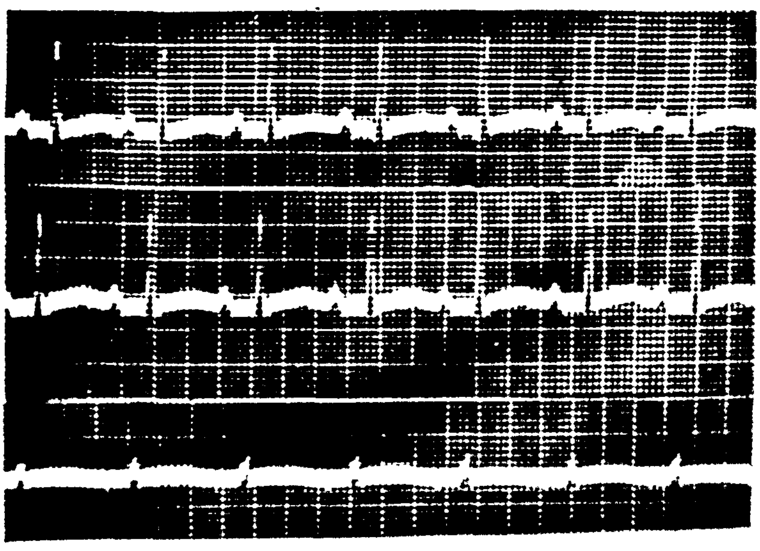

Fig. 6.—From the same patient nineteen days after Fig. 5. Note the return of the ventricular complexes toward normal.

cardiogram, but to accept this conclusion unqualifiedly seems unwarranted in the light of our observations. Furthermore, we are acquainted with no published case of rheumatic carditis showing definite

R-T deviation in which the question of pericardial effusion can be positively ruled out. Until such instances appear it seems to us that the question remains *sub judice.*

As stated above, we feel that our first case of hemopericardium is a clear example showing the effect of hydrostatic pressure in the pericardium on the ventricular complex of the electrocardiogram. The questions arise: First, what factors are concerned, and second, why is the R-T deformity in pericardial effusion so like that seen in recent myocardial infarction? These questions will be considered in detail in the paper dealing with our experimental observations on dogs. In brief, the functional effect of pericardial effusion is determined primarily by the hydrostatic pressure exerted on the heart—*Herztamponade.* This compresses the vascular channels and leads to anoxemia of the heart muscle. In addition the cardiac output is reduced, so that the coronary flow is impaired.

The hydrostatic pressure in the pericardium may vary widely in clinical cases because of such variable factors as (1) the element of time, i.e., the rate at which fluid accumulates in the pericardial sac, (2) the quantity of fluid—each further increment causing a greater elevation of hydrostatic pressure than the previous one, (3) the distensibility of the parietal pericardium—a given quantity of fluid in a rigid sac, e.g., tuberculosis of the pericardium exerting more pressure on the heart than the same quantity of fluid in a more elastic sac.

Referring now to the clinical curves, it is apparent that the later records from each case exhibit less deformity in the S-T segment than the earlier ones. In other words, as time elapsed the ventricular complexes became more normal in appearance. Assuming as we do, a direct relationship between hydrostatic pressure in the pericardium and anoxemia of the heart muscle, it follows that as the intra-pericardial pressure is lowered—by stretching of the parietal pericarduim or absorption and organization of the effusion—the anoxemic state of the heart muscle is relieved. On this basis the more nearly normal ventricular complexes found in the later records can be explained.

In conclusion we suggest that since the R-T deviation observed in coronary thrombosis occurs also in pericardial effusion, the term "coronary T-wave" is misleading and should, therefore, be discarded.

SUMMARY

Electrocardiograms from a case of hemopericardium and a case of purulent pericarditis with effusion are recorded which exhibit R-T deviations similar to those seen in recent myocardial infarction. These changes are ascribed to increased hydrostatic pressure in the pericardial sac which probably causes anoxemia of the heart muscle.

Observations on a case of rheumatic carditis showing abnormal ventricular complexes are included. In the interpretation of R-T deviation in rheumatic heart disease the presence of pericardial effusion must be considered.

The suggestion is made that since the R-T deviation observed in coronary thrombosis occurs also in pericardial effusion, the term "coronary T-wave" is a misleading one and should therefore be discarded.

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THE ELECTROCARDIOGRAM IN PERICARDIAL EFFUSION*

II. Experimental

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THE possibility that the electrocardiographic changes reported in our previous clinical paper are actually caused by pericardial effusion, was tested in experiments on normal dogs. For this purpose the experimental method described by Katz and Gauchat[1] was used. In brief, the dogs were anesthetized with morphine and barbitol, and artificial respiration instituted. A hole was made in the chest wall and a

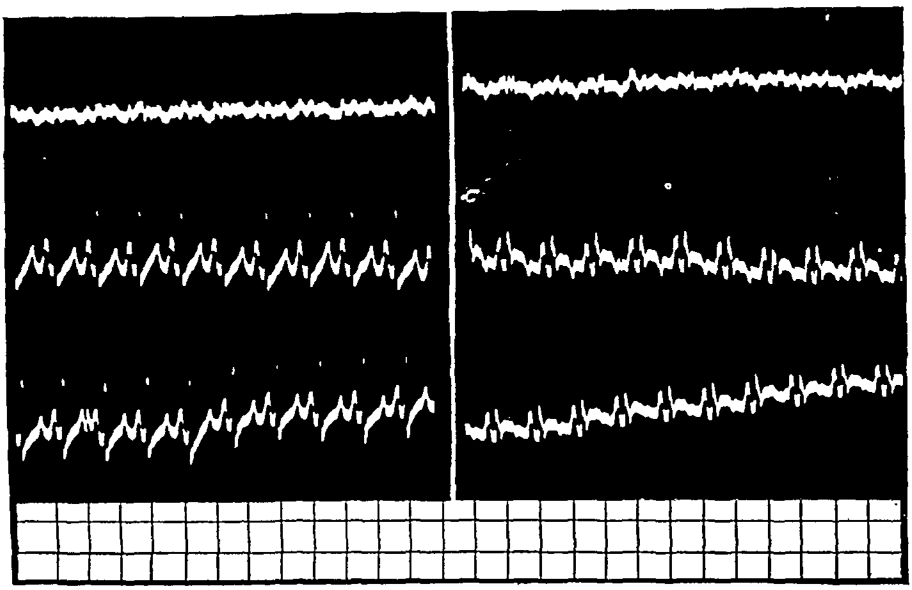

Fig. 1.—Electrocardiograms, three standard leads, showing the effect of acute experimental pericardial effusion. Segment on left, control; that on right, after 50 c.c. of isotonic saline were injected, and the pericardial pressure elevated to 220 mm. of saline. In this figure and succeeding ones, the scale at the bottom shows time in 0.2 second (ordinates) and voltage in 0.5 millivolts (abscissae).

specially constructed cannula was tied into the pericardium. Then the chest wall was repaired and a pleural cannula inserted, through which the pneumothorax was relieved. The cannula was now closed and normal respiration was resumed.

Electrocardiograms were obtained by the usual three leads and were standardized so that one centimeter was equivalent to one millivolt. The Victor electrocardiograph was used, its clockwork arranged to run 2.5 cm. per second. An electrocardiogram was taken after a certain amount of oil or isotonic saline had been forced into the pericardial sac by means of a 200 c.c. syringe, and the record compared with

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the control curves taken before the injection. The intra-pericardial pressure was registered with a U-tube manometer containing the same liquid used in the injection.

The principal changes observed in the electrocardiograms before and after experimental pericardial effusion are illustrated in Figs. 1, 2, 3, 4, and 5; in the legends of these figures are given the data concerning the amount of fluid injected and the resulting elevation in the pericardial pressure.

RESULTS

The following general effects are worthy of note. In some animals dyspnea was produced, in others apnea occurred following the pericardial effusion. In many instances the heart developed premature

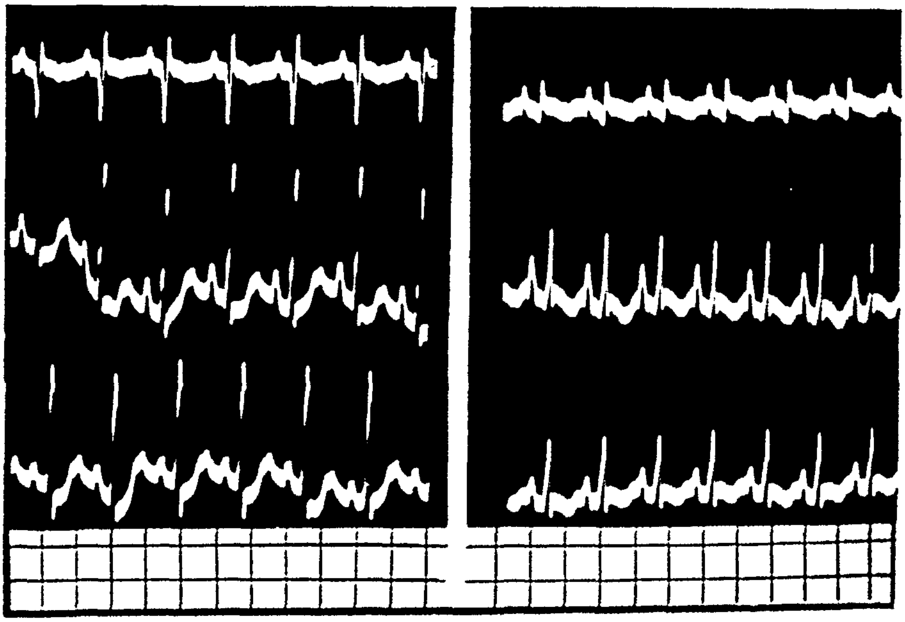

Fig. 2.—Three leads showing the effect of acute experimental pericardial effusion. *Segment on the left is control; that on the right, after 70 c.c. of oil were injected* into the pericardial sac and pressure raised 110 mm. of oil.

contractions, sinus bradycardia (see Figs. 3 and 4), or complete heart-block. These abnormalities disappeared as a rule when the fluid was removed. The pressure in the pericardial sac rose greatly, and as Katz and Gauchat[1] found, the respiratory undulations tended to disappear.

The electrocardiographic changes observed in the ventricular complex fall roughly into three categories:

1. The first type of R-T deviation resembles that found in our clinical cases and belongs to the so-called group of "coronary T-waves." It was found in four experiments on four animals out of a total of fifteen experiments on six dogs. The QRS complex becomes smaller in this type, the S-T segment does not shorten but is distinctly raised and is followed by a small inverted or upright T-wave. Three examples of this type are shown in all leads of Figs. 1 and 2, and in Lead II of Fig. 3.

In Fig. 1, Lead I, the voltage is so small that the changes are minimal. The changes in Leads II and III resemble each other. In both, the voltage of the QRS complex decreases, and slurring develops near the top of the descent of the R-wave; the S-wave does not quite reach the

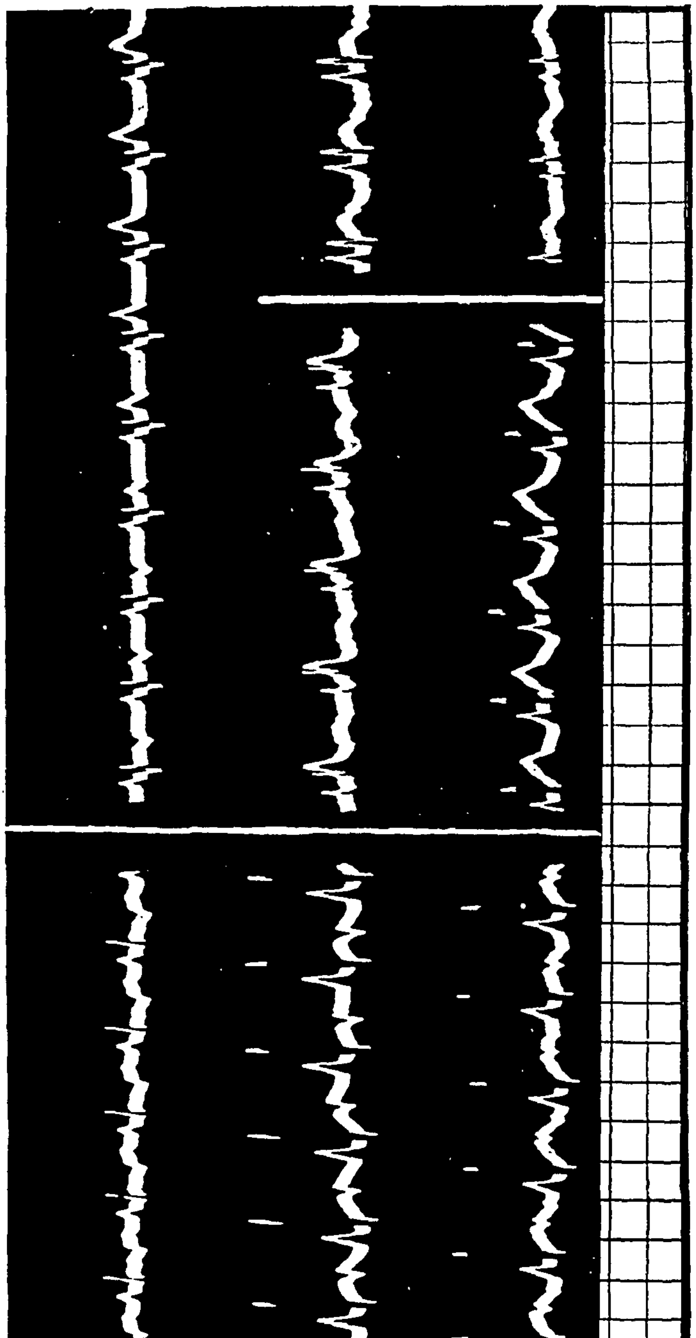

Fig. 3.—Three leads showing the effect of acute experimental pericardial effusion. Segment on the left, control; that in the *middle, after* 200 c.c. *of oil injected* and pericardial pressure elevated 165 mm. of oil. Note development of changes in Lead I, and also the different types of changes in the three leads. Segment on the right (Lead I omitted), after an additional 200 c.c. of oil were injected; the pericardial pressure now dropped to 180 mm. oil because a leak developed. The pressure was 140 mm. while Lead II was taken, and fell to 100 mm. as Lead III was recorded. Note the P-wave changes and the sinus bradycardia.

iso-electric level and is followed by a positive S-T segment, and this by a small negative T-wave. In Fig. 2 the changes in the S-T interval and T-wave of all three leads are similar to those of Leads II and III in Fig. 1. The QRS deflection becomes smaller in all leads; the negative

phase disappears in Lead I, becomes smaller in Lead III, and does not go below the iso-electric level in Lead II. In Fig. 3 the third segment of Lead II shows changes similar to those seen in Fig. 1. In the middle

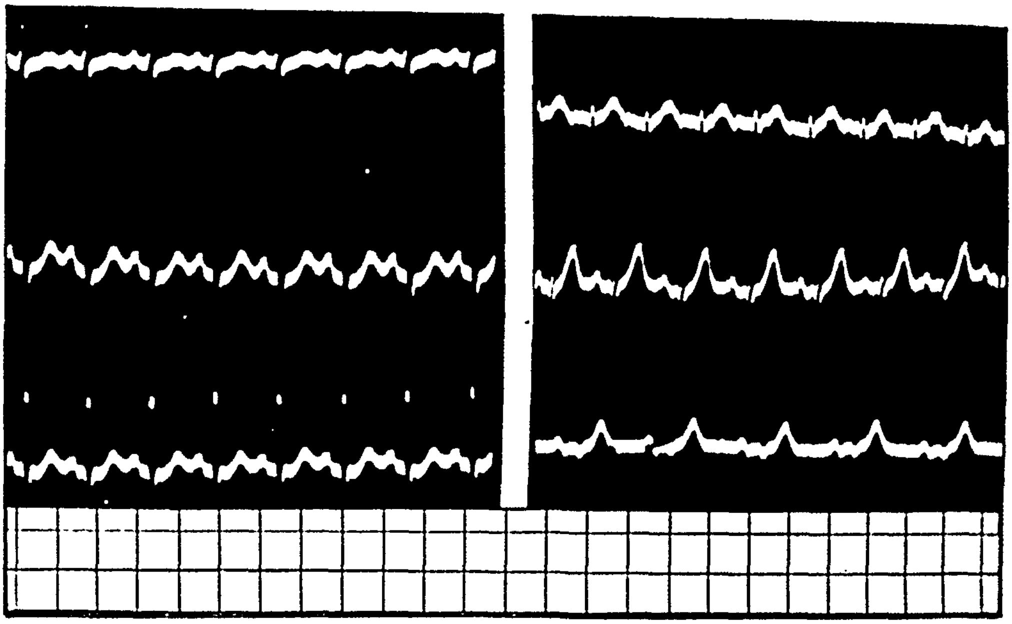

Fig. 4.—Three leads showing the effect of acute experimental pericardial effusion. Segment on left, control; that on right, after 180 c.c of isotonic saline injected and pressure in pericardial sac elevated to 320 mm. of saline. Note the P-wave changes and, in Lead III, the sinus bradycardia. White block in Lead II indicates height of R-wave in control record.

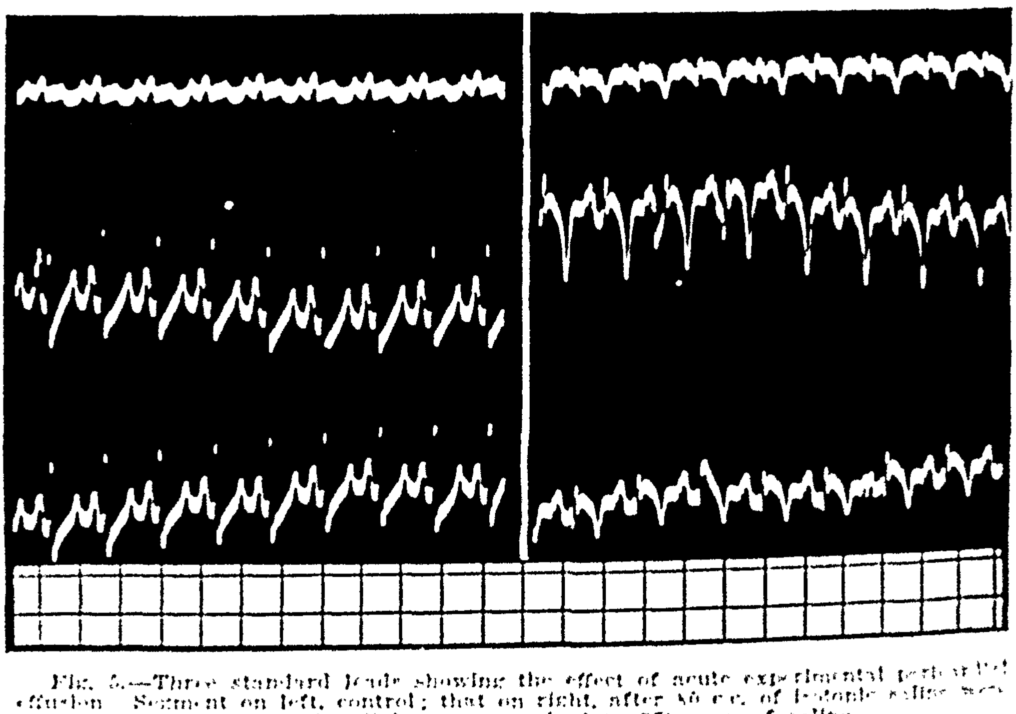

Fig. 5.—Three standard leads showing the effect of acute experimental pericardial effusion. Segment on left, control; that on right, after 80 c.c. of isotonic saline were injected and the intrapericardial pressure raised to 270 mm. of saline.

segment of Lead II (Fig. 3), the S-T interval is shortened and takes off high on the QRS group.

2. The second type of R-T deviation, shown in Leads I and III of Fig. 3, and in all leads of Fig. 4, was found in four experiments on two dogs. The QRS complex becomes smaller in this type also; the S-T interval shortens and its level remains unchanged or becomes slightly positive. The electrocardiogram is dominated by a rounded, broad, tall T-wave. The most typical change is seen in Fig. 4, especially in Lead II. Lead III of Fig. 3 shows two deviations of this type; in the last segment there is no shortening of the S-T interval and the T-wave is not very tall; in the middle segment the S-T interval is very short and the large T-wave is peaked. Lead I of Fig. 3 is very interesting because we were able to record the development of this type of change. It so happened that the record was taken inadvertently before all the fluid had been injected. The QRS takes on its final form in the first beat, but the T-wave is little changed; in the next three beats a small positive phase gradually develops in front of the negative one which gradually disappears. In the fourth beat a noticeable shortening of the S-T interval occurs which progressively becomes more marked in the succeeding beats, and the T-wave becomes more prominent.

3. The third type of R-T deviation is shown by eight experiments on two dogs. It is well illustrated in Fig. 5. The QRS complex becomes smaller in Leads II and III. The S-T interval does not shorten,* but becomes positive to varying degrees in the different leads. The dominant feature, however, is the deep inverted and peaked T-wave; note especially Lead II which is more typical of the usual change in this group.

It is significant that two types of deviation may occur in different leads of the same record, as in Fig. 3, or at different times in the same animal. For example, the curves in Fig. 1 and in Fig. 5 were obtained in different experiments on the same animal.

DISCUSSION

Such changes in the electrocardiogram as here recorded are not due to shifting in the axis of the heart, since the records of Cohn,[2] and Meek and Wilson[3] show no changes in the S-T interval or T-wave resembling those here described. Similarly, the relatively insignificant alterations found by Katz,[4] when the chest was opened and manometers inserted in the heart, rule out the possibility that the changes are due to short-circuiting. The decreased voltage of the QRS group was not due to insulation, as saline injections gave the same results as oil. It follows that these electrocardiographic changes must be due to the experimentally produced pericardial effusions, for they appear when the effusion is made and disappear when the effusion is removed. And

*In practically all the other instances, however, a distinct shortening of this phase is present.

the similarity of the experimental types to the clinical implies that the changes observed in our patients were in all likelihood due to the presence of fluid in the pericardial sac.

These experimental electrocardiographic changes, which resemble the clinical curves seen in recent occlusion of the left coronary artery can be explained on the basis that severe anoxemia of some regions of the left ventricle develops, causing a delay in the conduction of the impulse and a weaker response (mechanical and electrical) in the regions involved. In pericardial effusion the rapid accumulation of fluid in the pericardial sac causes an elevation of intra-pericardial pressure, which in our experiments reached in some cases 30 mm. of Hg. As shown by Katz and Gauchat[1] and by others, the pressure in the pericardium causes an elevation in the intra-ventricular, intra-auricular and venous pressures on both sides of the heart. In other words, with the tension of the heart musculature around zero, as happens during diastole, the wall of the heart is still under tension as a consequence of the hydrostatic pressure in the pericardium. An extra-vascular pressure is thus applied to the blood channels in the heart wall, causing a diminution in capillary flow such as appears normally during systole, as shown by Anrep.[5] Two other factors also tend to retard the blood flow through the heart. In the first place, an elevation of pressure occurs in the coronary sinus, as in the other veins emptying into the right auricle, and thus there results an increased resistance to outflow from the coronary capillaries. In the second place, the elevated pressure in the pericardium impedes the filling of the heart, thereby reducing the cardiac output together with the arterial blood pressure, i.e., the driving force of the coronary circuit is reduced. In short, pericardial effusion impairs the blood supply to the heart, causing a state of anoxemia, which apparently affects the left ventricle more than the right. This is suggested by the similarity of the curves in pericardial effusion to those seen in occlusion of the left coronary artery.

The variations in the experimental curves are probably due to differences in the location of the severe anoxemic areas of the left ventricle in the several experiments. Anoxemia does not affect the same regions to the same extent in different experiments, so that varying degrees of intra-ventricular block and decreased electrical response are combined. The combinations are such that roughly three groups of changes can be classified, as have been described.

SUMMARY

The effect of acute experimental pericardial effusion on the electrocardiogram was studied in normal dogs to ascertain whether changes would occur similar to those observed in our clinical cases reported in the preceding paper.

Three general types of abnormal ventricular complexes are classified. In all types the QRS complex becomes smaller in voltage. The groups differ in regard to the modification of the S-T segment and the T-waves as follows:

(a) The S-T segment in this group, which resembled the clinical cases, usually remained unchanged in duration but rose distinctly above the iso-electric level; the T-wave became small, usually inverted, but occasionally remained upright.

(b) The S-T segment in this group was shortened but usually remained at the iso-electric level, and the electrocardiogram was dominated by an upright, broad, tall and rounded T-wave.

(c) The S-T segment in this group was also shortened. As a rule, the level of this segment of the curve rose above the iso-electric level, but the striking feature was the development of a deeply inverted and peaked T-wave.

The hypothesis is suggested that the changes in the ventricular complexes of the electrocardiogram in experimental pericardial effusion are caused by anoxemia of the heart muscle which is more marked in certain regions of the left ventricle, leading to intra-ventricular block and diminished electrical response in the involved regions.

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ABNORMAL ELECTROCARDIOGRAMS IN PATIENTS WITH SYPHILITIC AORTITIS*†

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THE purpose of this communication is to present a detailed clinical and electrocardiographic study of 50 cases of syphilitic aortitis, some with and some without physical signs of aortic insufficiency. Certain differences in the electrocardiographic findings of these two groups have been discovered which are thought to be of diagnostic and prognostic importance. A similar series of 85 cases has been reviewed by Heimann,[1] who found 15 with downward T-wave in Lead II and 49 others with a "delay, or a delay and diminished amplitude" of T. Of his 85 records, 64 showed T-wave changes of some sort, though it is not quite clear what is meant by "delay" of T, and he did not specify how many showed this change alone. He called attention especially to the notching of QRS which was present in 25 of his cases (30 per cent), and which he believed was more commonly associated with syphilitic myocardial changes than with any other condition.

The patients selected for this study showed definite evidence of syphilis in a positive history of a chancre, a positive Wassermann reaction, x-ray evidence of aneurysm or diffuse dilatation of the aorta in a young individual, or definite syphilitic lesions in another part of the body or in the aorta at post-mortem examination. Some showed only two of these features, but many of them showed more than two. In the least definite case the evidence rested upon a dilated aorta, and although the Wassermann was negative, there was a cutaneous lesion which was positively diagnosed as syphilitic, by Doctor A. B. Cannon of the dermatological service.

The group showing aortitis without insufficiency, Group 1, consisted of 16 cases; 15 of these were males and the other a female. The group showing aortitis with aortic insufficiency, Group 2, consisted of 34 cases; 28 were males and 6 females. The age distribution in these groups is shown in Table I. It will be noted that the group with aortic insufficiency is on the whole composed of somewhat older individuals than the group without this lesion. The serological tests are shown in Table II. The blood Wassermann reaction was positive in 86 per cent of all the cases, but only 5 cases or 10 per cent were nega-

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This report is part of the study of cardiovascular syphilis undertaken on behalf of the Committee for the Coordination of Investigation of the American Heart Association.

†Read at the Fifth Annual Scientific Session of the American Heart Association, Portland, Oregon, July 9, 1929.

tive both as to blood and as to spinal fluid serology. The symptoms of which the patients complained are shown for the two groups in Table III. In the group without aortic insufficiency the equal frequency of

TABLE I

AGE DISTRIBUTION

YEARS	GROUP 1	GROUP 2 (AORTIC INSUFFICIENCY)
32 - 39	6	4
40 - 49	6	13
50 - 59	2	15
60 - 68	2	2

TABLE II

SEROLOGY

	GROUP 1	GROUP 2 (AORTIC INSUFFICIENCY)
Blood Wassermann Positive	12	30
Blood Wassermann Negative	2	3
Blood Anticomplimentary	1	–
Spinal Fluid Colloidal Gold Luetic Curve	1	1

TABLE III

SYMPTOMATOLOGY

	GROUP 1	GROUP 2 (AORTIC INSUFFICIENCY)
Tumor of the Anterior Chest	3	–
Hoarseness	2	1
Pain in the Anterior Chest	7 (44%)	13 (38%)
Pain in Both Shoulders	1	–
Pain in the Left Shoulder	2	–
Pain in the Left Arm	1	–
Pain in Left Side of Chest	1	–
Pain in Right Side of Chest	2	–
Pain in Back	3	–
Pain in the Epigastrium	1	4
Dyspnea	7 (44%)	26 (77%)
Edema	3 (19%)	9 (27%)
Weakness	2	4
Palpitation	1	6
Cough	1	2
Hemiplegia or Aphasia	–	44
Pulsation in Neck	–	2
Dysphagia	–	1
Epistaxis	–	1
Choking Sensation	–	1

shortness of breath and pain in the anterior chest is interesting, but if pains in the shoulder, arms, sides of the chest and back are also considered, it will be seen that pain of one sort or another is by far the most frequent symptom in these patients. In the group with aortic insufficiency the predominant symptom is shortness of breath, although pain in the anterior chest occurs with considerable frequency.

Edema is also a frequent symptom in this group; it occurred nine times, or in 27 per cent of the cases. This shows how advanced are the cardiac symptoms when these patients come to the hospital for treatment. In Table IV only the chief complaint is considered. Here we see as in Table III that patients without aortic insufficiency complain chiefly of pain; those with it complain chiefly of shortness of breath, although pain sometimes accompanies this.

TABLE IV

CHIEF COMPLAINTS

	GROUP 1	GROUP 2 (AORTIC INSUFFICIENCY)
Pain in the Back	2	–
Pain in the Anterior Chest	6*	2
Pain in the Chest and Dyspnea	4	12
Dyspnea With or Without Edema	3	12
Weakness	1	1
Palpitation	1	
Hoarseness and Dysphagia	1	
Aphasia	1	
Hemiplegia	–	2
Cough and Palpitation	–	1
No Cardiac Symptoms	–	1†

*In two cases the pain radiated to the arms.
†Entered hospital for inoperable carcinoma of cervix.

TABLE V

PHYSICAL EXAMINATION

	GROUP 1	GROUP 2 (AORTIC INSUFFICIENCY)
Tracheal Tug	1	–
Palpable Tumor		
Anterior Chest	7	–
Posterior Chest	1	–
Stridor	2	–
Systolic Murmur at the Apex	4	19
Systolic Murmur at the Base	4	33
Aortic Diastolic Murmur	–	34
Aortic Second Increased	1	–
Blood Pressure Normal or Less	14	19
Blood Pressure Increased	2	15
Corrigan Pulse	–	14
Large Pulse Pressure	1	34
No Abnormality Except by X-ray	2	

In Table V is an analysis of the chief findings on physical examination. In the group without aortic insufficiency, murmurs over the cardiac valve areas are infrequent, and in this group also a normal blood pressure is common. In the group with aortic insufficiency a systolic murmur at the base occurs in almost every case, as well as the diastolic murmur of aortic insufficiency. Table VI shows the results of the x-ray examination of these patients. Every patient with aortic insufficiency showed a diffuse dilatation of the aortic arch. Five of these patients also had aneurysm. Cardiac enlargement was diagnosed in all except

TABLE VI

X-RAY FINDINGS

	GROUP 1	GROUP 2 (AORTIC INSUFFICIENCY)
Aneurysm of Aorta	11*	5
Diffuse Dilatation of the Arch	4	34
Cardiac Enlargement	8	33
"Duck-back" Appearance Typical of Aortic Insufficiency	–	22
Heart Not Enlarged	8	1†
Enlarged to the Right	2	18

*One case was not examined by x-ray, but showed aneurysm of the innominate artery at autopsy.

†This heart was reported "not enlarged but suggesting concentric hypertrophy."

TABLE VII

ELECTROCARDIOGRAPHIC FINDINGS

	GROUP 1	GROUP 2 (AORTIC INSUFFICIENCY)
Premature Beats	4	3
Auricular Fibrillation	–	3
Prolonged A-V Conduction Time	1	1
Right Axis Deviation of QRS	1	–
Left Axis Deviation of QRS	9 (51%)	31 (91%)
Neither Right nor Left Axis Deviation	6 (38%)	3 (8 %)
QRS Group		
Abnormal Duration	1	10
Notched or Slurred	3	10
Low Voltage	1	–
Unusual Peculiarity	2	2
High Voltage	2	11
Total Significant Abnormalities	6 (38%)	14 (41%)
T-Wave		
Downward in Lead I	4	9
Downward in Lead II	–	2
Downward in Leads I and II	–	15
Diphasic in Lead I	1	1
Diphasic in Leads I and II	–	2
Low Voltage	1	–
"Coronary" Type	1 (7 %)	8 (21%)
Total Abnormal T-Wave	6 (38%)	29 (85%)
No Significant Abnormality of QRS or of T	6 (38%)	5 (15%)

one of this group, but this one patient was said to show a concentric hypertrophy by the exaggeration of the left ventricular curve. In the group without aortic insufficiency cardiac enlargement was only diagnosed in half of the cases.

Table VII presents the electrocardiographic findings in the two groups. It will be noted that auricular fibrillation occurred only in the group with aortic insufficiency, and that many cases in the other group showed neither right nor left axis deviation of QRS. Left axis deviation of QRS was much more frequent in the group with aortic insufficiency, and 85 per cent of these patients showed an abnormality of QRS or of T which was considered significant of myocardial damage.

Only 62 per cent of those without aortic insufficiency had significant abnormalities in their records.

Abnormalities of the QRS group occurred with about equal frequency in those with and those without aortic insufficiency. Heimann[1] unfortunately did not describe the exact features of the notching of QRS which he found in 30 per cent of his series, and to which he attached so much diagnostic importance. Our series, however, showed only 7 records which resembled the notch of his illustration. Notching of the usual sort occurred in 13 of the records of our series, which is 26 per cent, or about the same frequency of occurrence as he described for the special form of notching. Notching occurred in 20 per cent of our cases without aortic insufficiency, and in 30 per cent of those with the lesion. Abnormalities of the T-wave occurred, however, in 85 per cent of those with aortic insufficiency, and in only 38 per cent of those without this lesion. The T-wave was of the "coronary" type[2] in 21 per cent of the group with insufficiency, and in only one case, 7 per cent, of the other group.

Seven patients without aortic insufficiency and 12 with it failed to recover. The mode of death is shown in Table VII-A. Although cardiac decompensation was the predominant cause in both groups, yet it was of much greater frequency in the patients with valvular disease. The deaths in the group with aortic insufficiency all occurred in patients who showed an abnormal T-wave in the electrocardiogram. All of the patients in this group who had normal T-waves recovered sufficiently to be discharged from the hospital, and it is possible that their recovery depended, in part at least, upon the absence of serious coronary or myocardial involvement as suggested by the normal T-wave.

Autopsies were obtained in 4 out of 12 of those patients with aortic insufficiency who died in the hospital, and on 6 out of the 7 without the lesion. The autopsy findings are shown in Table VIII. It will be seen that 2 patients who had aortitis but did not have physical signs of aortic insufficiency, showed a thickening of the valve cusps.

Table VII-A

Mode of Death

	Group 1	Group 2 (Aortic Insufficiency)
Decompensation	3	8
Bronchopneumonia	1	2
Anginal Attack	–	1
Carcinoma of Cervix	–	1
Tracheal Pressure	1	–
Rupture of Aneurysm	2	

It appears from this that the valves must be involved to a certain definite degree before they become incompetent. Just as in the x-ray study, so also the autopsy revealed that half of the hearts without the

valvular lesion were enlarged, and half were of normal size, while in the group with the valve lesion, all were enlarged. Syphilitic narrowing of the mouths of the coronary arteries was observed in each patient with aortic insufficiency but was not found in any of those without this valve lesion.

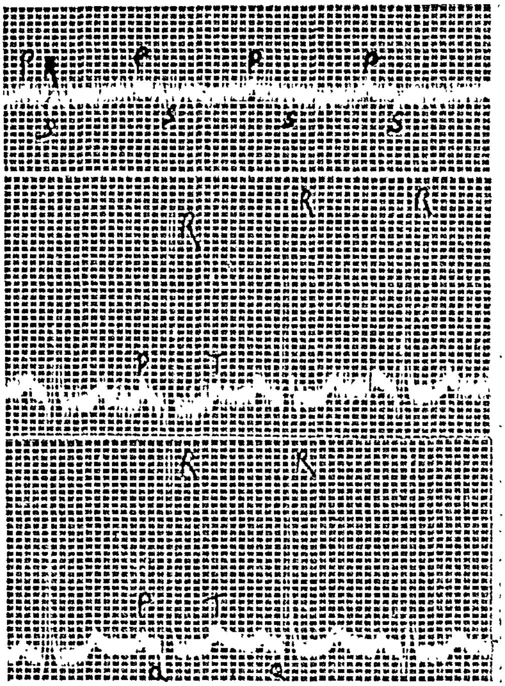

Fig. 1.-*A*.

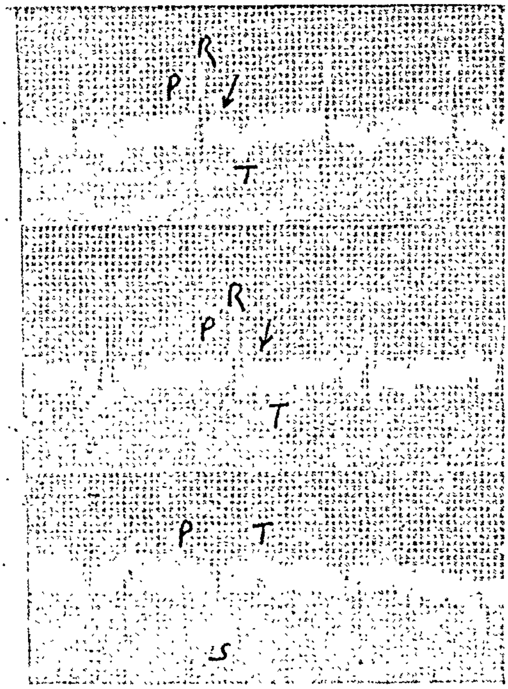

Fig. 1-*B*.

Fig. 1.—Electrocardiograms of Case 2, *A*, and Case 7, *B*, of the autopsy series Tables VIII and IX. Note in *A* the normal appearance of the electrocardiogram with a borderline right axis deviation of QRS, and in *B* the notching of the QRS group and the inversion of T in Leads I and II, with the coronary feature—the upward convexity indicated by the arrow—in both of these leads.

Fig. 2-*A*.

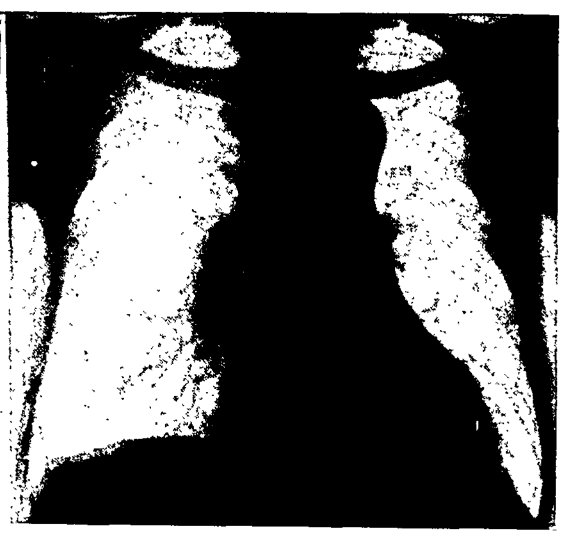

Fig. 2.-*B*.

Fig. 2.—Teleroentgenograms of Case 2, *A*, and Case 7, *B*, of the autopsy series, Tables VIII and IX. Note in *A* the small heart and the large aneurysm which involved the ascending portion of the arch. In *B*, note the dilated and somewhat tortuous aortic arch.

It will be interesting to consider the electrocardiographic abnormalities which were found in records from the autopsied cases. These are shown in Table IX. It will be noted that Cases 4, 5, and 6 of the group without aortic insufficiency showed an abnormality of the T-wave. No pathological changes were found to explain this abnormality in Case 4, but Case 5 showed arteriosclerosis of the coronary arteries and marked vascular renal disease. Case 6 also showed marked vascular renal disease, and it was thought that in these two cases the T-wave abnormality might be due to arterio-sclerotic changes in the smaller coronary branches. All of the cases with aortic insufficiency showed T-wave abnormality. Case 9 also showed marked vascular renal dis-

TABLE VIII

AUTOPSY FINDINGS

CASE	1	2	3	4	5	6	7	8	9	10
Syphilitic Aortitis Without Aneurysm						x		x	x	x
Syphilitic Aortitis With Aneurysm	x	x	x	x	x		x			
Aortic Valves, Normal	x	x	x	x						
Aortic Valves, Thickened					x	x	x	x	x	x
Aortic Insufficiency							x	x	x	x
Syphilitic Involvement of Coronary Mouths							x	x	x	x
Marked Vascular Renal Disease					x	x			x	
Arteriosclerosis of Coronaries Without Occlusion	x				x					
Heart Enlarged			x		x	x	x	x	x	x
Heart not Enlarged	x	x		x						
Brown Atrophy	x	x								
CAUSE OF DEATH										
Rupture of Aneurysm	x		x							
Bronchopneumonia		x								
Tracheal Pressure				x						
Cardiac Failure					x	x	x	x	x	x

TABLE IX

ELECTROCARDIOGRAPHIC FINDINGS IN AUTOPSIED CASES

CASE	1	2	3	4	5	6	7	8	9	10
Premature Beats				x	x					
Prolonged A-V Conduction			x							
Right Axis Deviation of QRS		x								
Left Axis Deviation of QRS	x			x	x		x	x	x	x
Neither Right nor Left			x			x				
QRS Group										
Abnormal Duration							x	x		x
Notched or Slurred					x		x	x	x	x
Low Voltage			x							
High Voltage		x							x	x
T-Wave										
Downward in Lead I				x	x	x				x
Downward in Leads I and II							x	x	x	
"Coronary" Type					x		x			
No Significant Abnormality of QRS or of T	x	x								

ease, but the other 3 did not. It is believed that the T-wave changes of these 3 cases were due to the syphilitic narrowing of the mouths of the coronary arteries, which was demonstrated at autopsy.

Syphilis produces characteristic changes in the aorta. These may be described briefly as an infiltration about the vasa vasorum of the adventitia and media by wandering cells of the character of lymphoid and plasma cells with sometimes multinucleated giant cells. The elastic fibers of the media become necrotic, and diffuse scarring of this coat takes place. The intima becomes thickened and longitudinally wrinkled, and the entire vessel wall is thinned and weakened to a considerable extent, the end-result being either a diffuse dilatation or aneurysmal sac formation. This process usually begins in the ascending aorta, a few centimeters above the aortic ring, and spreads both upward and downward. As the process advances the mouths of the smaller branches of the aorta are inevitably encroached upon. It is evident from Cases 5 and 6 of our autopsied series that the process may descend far enough to involve the aortic valve, and yet the coronary orifices may not be grossly narrowed. Nine such cases were found by Clawson and Bell[3] in a group of 126 autopsies on patients with syphilitic aortitis. It is also conceivable that the coronary orifices might become involved when the aortic valves were still at least approximately normal. Such a case has been reported by Dr. H. S. Martland, associated with a congenitally high position of both coronary arteries, and 21 cases were found by Clawson and Bell in their series. Coronary narrowing by luetic aortitis must lead to a defective nutrition of the heart muscle, and this we believe is the cause of the abnormalities found in the electrocardiograms of our patients with aortic insufficiency.

The careful histological studies made by Clawson and Bell[3] of a group of patients clinically similar to ours revealed a narrowing of one or both coronary orifices in 22 of 28 cases with aortic insufficiency (79 per cent), but a study of the myocardium of these 28 cases revealed only microscopic fibrosis or proliferative reaction in 11 (39 per cent). Since we have found changes in the T-wave in 85 per cent of such cases, and histological changes are found in only 39 per cent, it is evident that the T-wave abnormality must often depend upon changes in the muscle physiology due to coronary narrowing but without demonstrable histological basis. These authors found narrowing of the coronary orifices in 3 of 23 patients with aneurysm of the aorta, and in 4 others of the 23 there was either microscopic fibrosis or a proliferative reaction. This is a much smaller incidence of both coronary and myocardial damage than in the group with aortic insufficiency, and is so small as to make us wonder why we found 62 per cent of abnormal electrocardiograms and 38 per cent incidence of T-wave abnormality in our group without aortic insufficiency. Here again the T-wave abnormality may depend upon myocardial changes which do not have a demonstrable pathological basis.

SUMMARY

Of 50 patients of syphilitic aortitis which were studied, two-thirds had aortic insufficiency and one-third did not; about one-third had aneurysm; 5 had both aortic insufficiency and aneurysm.

In general the patients with aortic insufficiency were older than those without; shortness of breath was their chief complaint, though pain in the anterior chest was frequent, and almost one-third complained of edema. All but one showed a systolic murmur at the aortic area.

The electrocardiogram showed an abnormal T-wave in 85 per cent of these patients, and in 20 per cent it was of the "coronary" type. It was abnormal in only 38 per cent of those without the valve lesion, and only 1 case (7 per cent) showed a wave of the "coronary" type.

Ten autopsies were obtained on these 50 cases, and from a study of the autopsy material and the electrocardiographic records it appeared that the abnormality of the T-wave is probably due to encroachment upon the lumen of the coronary orifices by the syphilitic disease in the sinuses of Valsalva. The greater frequency of the T-wave changes in the group with aortic insufficiency is due to the fact that in these patients the aortitis involves the region of the valves near which the coronary arteries originate.

Changes in the T-wave of patients with syphilitic aortitis should be viewed as an indication of serious coronary involvement, but not necessarily as an indication of myocardial pathology.

This observation has an extremely important bearing upon our general understanding of the causes of abnormality of the T-wave.

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(For discussion, see page 115.)

SYPHILITIC CORONARY OCCLUSION IN AORTIC INSUFFICIENCY*†

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IMPAIRED circulation resulting from disease of the coronary arteries causing symptoms, heart failure and death is receiving an increasing amount of attention since Obrastzow and Straschezko in 1910,[1] and Herrick in 1912,[2] called attention to the syndrome accompanying the sudden occlusion of these arteries. Since this condition is being recognized more generally by the profession, the frequency with which it occurs indicates that it is probably a far more common lesion than has been suspected in the past. Those factors, therefore, having a causal relation to coronary disease, whether predisposing to the precipitation of clots, proliferation of the intima, atheroma, or any other change becomes of prime importance. Syphilis has long been recognized as causative in certain cases. It is this condition that I will discuss, presenting two case reports and a syndrome which I believe will permit of recognition in certain cases.

The first observations on coronary disease seem to have been made by Drelincourt (1700),[3] and the association of coronary and myocardial disease was first noted by Bellini (1703).[3] Later Edward Jenner[4] and also Parry[4] believed disease of these arteries to be the underlying lesion in angina pectoris, though Allbutt insisted that what Jenner really said was that, in patients dying of angina, coronary sclerosis would be found, which he felt was quite a different matter.

Involvement of the aorta by syphilis, resulting in aneurysm [a relation suspected by Paré[5] and later insisted upon by Lancisi (1728) and Morgagni (1761)[5] and established by Welch, (1876), Dohle (1888)[5] and confirmed by others] and also the deformity and destruction of the aortic valve resulting in insufficiency (so well described by Dominick Corrigan in 1832)[6] are common conditions in the southern negro. The combination of aortic insufficiency with coronary closure is commented upon by most authors as of frequent occurrence. Benson states that syphilitic occlusion accounts for most closures of the coronaries and that the effect on the heart is similar to other gradual closures of these vessels where sufficient time has elapsed for anastomosis with the other coronary to develop. According to Stokes,[7] in

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advanced grades of involvement of the aortic valve the encroachment on the coronaries may be expected to be severe. The symptoms may not be a guide, for even in mild grades of aortitis coronary change may be so severe as to menace life.

Osler in his Lumelian Lecture[8] stated, "A man may get on very comfortably with practically a fourth of the whole coronary system," and Allbutt[9] goes even farther and says that, "a man may get on with the whole system occluded, so far, at any rate, as the orifices and main trunks are concerned," and concluded with Kanthack that other things being equal, the factor of safety is the rate of occlusion.

The following case reports illustrate certain features of interest:

CASE REPORTS

CASE 1.—E. E., well-nourished colored female, 26 years old, admitted January 22, died January 24, 1927. Stated that three weeks prior to admission she developed a cough, slight sore throat and soreness through her chest. One week later she developed shortness of breath and swelling of feet and legs. She had leucorrhea but denied venereal lesion. History otherwise not relevant.

Physical Examination.—Temperature 97°; pulse ranged between 88-130; respiration 28-44, labored and shallow; blood pressure, systolic 120 mm., diastolic 50 mm.; mucous membranes of mouth and throat congested; veins of neck prominent; râles in lower lobes of both lungs posteriorly; cardiac dullness to sixth interspace, 12.5 cm. to left of midsternal line. Apex not visible, soft systolic murmur at apex poorly transmitted. No signs of fluid in abdomen, which was distended and tympanitic. Some swelling of feet and ankles. Hemoglobin 50 per cent. Red blood cells 2,100,000, leucocytes 9,000, 52 per cent polynuclears; catheterized urine—acid, specific gravity 1.010. Acetone 1 plus, otherwise negative. Wassermann, Kolmer antigen, plus 4.

Autopsy.—This subject was a young negro woman, about 26 years old, about 5 feet tall, weighing about 100 lbs., in well-nourished condition.

There was a moderate anasarca, most noticeable in the legs and neck and general evidence of chronic heart failure in general marked passive congestion, edema, tissue degeneration and fibrosis, this being particularly in evidence in the lungs, liver and spleen. The kidneys showed merely cloudy swelling. The uterus was infantile, and there were bilateral dermoid cysts of the ovaries, each the size of a large orange. There was no arteriosclerosis.

The aorta was pliable and elastic everywhere except in two areas. One of these was just distal to the aortic orifice and included a part of one of the aortic valve cusps. The other was up in the arch of the vessel. These areas were quite similar in appearance, the proximal one being roughly pear-shaped and occupying about one square inch of intimal surface. It began just behind the left posterior cusp, involving this cusp, and through its center coursed the completely obliterated mouth of the left coronary artery. The higher area was roughly rounded and about twice the size of the first. These areas were raised above the intimal level almost one fourth of an inch, were firm and of cartilagenous consistency. They were of a hyaline pale bluish appearance depressed and yellowish in the center. Over their surfaces were rough lines generally paralleling the course of the vessel. There were a few yellow atheromatous patches at other points in the intima. Microscopically, these areas are of typical syphilitic aortitis, with prominent vasa vasorum in the outer coats surrounded by lymphocytes, patches of necrosis in the media and marked hyaline fibrous thickening of the intima.

The heart was extremely soft and flabby, a collapsing "dish-rag" heart. The cavities were dilated but there was little or no hypertrophy. On section the muscle wall could be seen to have fibrous strands through it. There was slight thickening of the margins of the mitral leaflets. One cusp of the aortic valve was thickened, stiff, retracted and bound down into the syphilitic lesion about its base, as described above, giving definite valvular insufficiency. Microscopically some of the muscle of the heart wall showed definite, but not outstanding hypertrophy. There was general fibrosis, congestion and parenchymatous degeneration. Near the endocardium was extreme parenchymatous and fatty degeneration and fibrosis. The coronary vessels were open except as described above at the mouth of one main artery.

The disability in this case plainly was the result of the syphilitic lesion at the aortic ring, giving slowly progressive aortic insufficiency and at the same time, gradually closing the mouth of the involved coronary artery. This nutritional impairment of the heart prevented the ordinary response of cardiac hypertrophy and led to a failure of the heart, unusually rapid in progress to completeness.

CASE 2.—M. G., Colored female, 26 years old, entered October 14, died, October 19, 1927. For three months, she had noticed palpitation and shortness of breath aggravated by exertion. Forced to stop all work two weeks prior to admission. Feet, legs and abdomen began swelling ten days before admission. Three children living and well, no miscarriages. No history of initial sore. History otherwise not relevant.

Physical Examination.—Temperature ranged from 96°-99°, reaching 100.5° the day before death. Pulse averaged 120. Respiration averaged 26 but was labored and shallow. Blood pressure 114 mm. systolic, 46 mm. diastolic. Heart not apparently enlarged; apex in fifth space 8 cm. to left of midsternal line. Thrill over precordium corresponding to to-and-fro murmur; moderate general edema. Hemoglobin 75 per cent, red blood cells 3,800,000; white blood cells 34,000; polynuclears 80; Wassermann plus 4; catheterized urine—acid, specific gravity 1.010, albumin plus 1; casts, hyaline plus 1; finely granular plus 2; otherwise negative. Blood culture negative.

Autopsy.—This subject was a negro woman about 26 years of age, of good development and state of nourishment and with marked general edema, anasarca, ascites and some excess fluid in pleural and pericardial cavities. There was general evidence of chronic heart failure in passive congestion, edema, tissue degeneration and fibrosis, this being prominent in lungs, liver, spleen and kidneys. There was a well-marked sclerosis with calcification of the walls of the small arteries in the uterus, and this organ was fibrous. The ovaries contained several small cysts. The kidneys showed some sclerosis of small arteries with some glomerular fibrous obliteration, patchy cortical fibrosis with lymphocytosis.

In the first part of the aorta, involving two cusps of the aortic valve and the mouth of the right coronary artery was an elevated, bluish, hyaline plaque, with rough and striated center. The valve cusps were thickened, uniformly shortened, retracted, and were agglutinated to each other at their adjoining ends. The mouth of the involved coronary was completely closed and the lumen obliterated by fibrosis to the first branch. The remainder of the coronary system was open. Section of this area in the aortic wall showed characteristic syphilitic aortitis, with fibrous thickening and surrounding lymphocytosis of the vasa vasorum, degeneration, necrosis and pronounced fibrosis of media and intima.

The heart was little if at all hypertrophied, some of its fibers being large on section. The musculature was extremely flabby and pale, and the cavities were

dilated. The muscle fibers generally were granular and near the endocardium very markedly vacuolated. Here particularly, were marked congestion and fibrosis. The capillaries generally were engorged with blood and along their courses were many polynuclear leucocytes. There were some diffuse fibrosis and noticeable mononucleosis. Beneath the epicardium, especially at the base posteriorly, were numerous petechial hemorrhages.

This heart could be reasonably called that of chronic myocarditis, or carditis, since all its parts were involved in a process which was more than the ordinary degeneration and fibrosis. While the state may be one of syphilitic carditis. it appears that the main condition and disability was the result of the syphilitic lesion at the aortic ring with resulting aortic valve insufficiency and a coincident occlusion of the mouth of one coronary artery, again so handicapping the organ as to bring about a progressive failure to completion in a period of time and with a rapidity of development of signs of cardiac failure different from simple aortic insufficiency, even of such origin.

These two cases were selected as the basis for this report because of their striking similarity in so many features. In each case the age was 26 years. While it is generally accepted that the time elapsing from the chancre to the development of the aortic leak averages from 18 to 20 years, it is also well known that this is not always the case. Brooks[10] reports 5 cases in patients under 30 years of age and states that they showed a most striking and extensive coronary involvement.

The patients here reported were both women. In a series of 146 consecutive cases recently admitted to the cardiovascular service of Roper Hospital, there were 83 males and 19 females. Both of the cases reported here were colored. The course was rapid in each case, 3 weeks and 3 months respectively. It is possible that the patients may have been sick longer than they stated, and that they dated the onset from the time they noted disabling symptoms. However, as Allbutt[11] states, "For I would repeat that the course of cardio-aortic syphilis combined, as it too often is, with coronary disease may be stealthily swift. Indeed, it is a kind of microbic endocarditis." Brooks[12] records a case of perforation of one of the coronary sinuses before the secondary rash appeared.

The systolic blood pressure was not elevated, but the diastolic was low, resulting in an increased pulse pressure, 114-46 in one, and 120-50 in the other. The respiration in each of these cases was notable for being labored rather than for rapidity, averaging around 27 in one case, and 35 in the other.

The Wassermann reaction was positive (plus 4) in each and was 89 per cent positive for the group of 38 colored women in our series, while for the 6 white women of the group, there were only 33 per cent positive reactions. The percentage of positive reactions for the group of 146 cases was 82 per cent, 48 per cent for the white and 89 per cent for the colored.

The post-mortem examination disclosed syphilitic aortitis with aortic insufficiency in each case. Allbutt[13] states that aortic valve involvement would appear to be present in about 30 per cent of all cases of syphilitic aortitis, mild and severe. Arneth in 202 cases of tertiary syphilis states he found 3.2 per cent of aortitis and 2 per cent of aortic regurgitation. In our series, the diagnosis of incompetency of the aortic valve was made 51 times in about 35 per cent of all cases *or* of cases with aortitis. Some of these cases were readmissions, but if we take the actual number of new cases, 107, aortic insufficiency was present in 23 cases (21 per cent).

Both these cases had a main branch of the coronary occluded at the ostium; in one, the right branch, and in the other, the left. All authors agree that this is common in aortitis, though I could not find any figures quoted. G. A. Allen,[13] in analyzing 1,000 consecutive postmortems, found macroscopic lesions of the coronaries in 371 cases. In 97, there was definite narrowing or blocking of the lumen, only 7 of which were due to syphilis. According to Allbutt[11] the right is usually first involved, and he quotes Broadbent as insisting that this is the reason that cases of syphilitic aortic insufficiency do badly. Clinically, there was no appreciable difference in the two cases suggesting any variation depending on which artery is occluded. The patient with blocking of the left artery was sick only three weeks and showed much more congestion of the mucous membranes of mouth and throat and dilated neck veins; the one with the occlusion of the right branch was sick three months and showed more anasarca and ascites.

Each of these two cases failed to exhibit the usual response to incompetency of the aortic valve with hypertrophy. Whether this was due to the lack of a normal myocardium as postulated by Krehl[14] or to the lack of adequate nutrition due to blockage of the coronary is questionable. Personally, I think the latter is more likely and that the impaired nutrition itself contributed to a more rapid degeneration of the muscle and the absence of hypertrophy. It is regrettable that owing to the stress of routine, these sections were not stained for the spirochete. There is much in the picture to suggest that they would have been found.

SUMMARY

Two cases of syphilitic aortitis with insufficiency and occlusion of a main branch of a coronary artery are reported. The striking similarity of the cases is commented upon, and statistics from analysis of a small series of cases are utilized.

It would seem therefore that in young adults with syphilis and aortic insufficiency who do not exhibit the usual compensatory hypertrophy and whose progress is rapidly toward a fatal outcome, one may reasonably presume the involvement of one or more of the coronary openings in the syphilitic process.

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(For discussion, see page 115.)

THE INCIDENCE OF HEART DISEASE IN THE PACIFIC NORTHWEST*

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WITH increasing interest in heart disease it is apparent that certain cardiovascular lesions may be more prevalent in one part of the country than in another. It has been shown that acute rheumatic fever is more prevalent in rigorous climates than in equable ones.[1, 2, 3] Syphilis in a charity hospital in the South is more common (largely because of negro admissions) than in other localities.[4] In regions where goiter is endemic the cardiovascular symptoms due to this condition can be studied to advantage. One would expect the more common forms of heart disease, such as those associated with arterial hypertension, to be equally distributed regardless of locality. A comprehensive report of the work recently carried out in New York State[5] serves as an example of the value of local studies.

In attempting a study of the incidence of heart disease in the Pacific Northwest, we are aware of the size of the problem and the inadequacy of material for careful and comprehensive statistical value but have obtained, we think, a preliminary cross-section of the material at hand.

For comparison with other parts of the country as to mortality from all causes and mortality due to diseases of the circulatory system, the following tables are presented:†

TABLE I

DEATH RATE PER 1000 DUE TO ALL CAUSES

OREGON	CALIFORNIA	WASHINGTON	MAINE	NEW YORK
Average for 10 yrs. to 1927	Average for 9 yrs. to 1926	Average for 9 yrs. to 1926	Average for 9 yrs. to 1926	Average for 9 yrs. to 1927
11.4	14.2	10.52	13.8	13.7

TABLE II

DEATH RATE PER 1000 DUE TO DISEASE OF THE CIRCULATORY SYSTEM

OREGON	CALIFORNIA	WASHINGTON	MAINE	NEW YORK
Average for 10 yrs. to 1927	Average for 9 yrs. to 1926	Average for 7 yrs. to 1926	Average for 7 yrs. to 1926	Average for 7 yrs. to 1926
1.9	2.62	1.62	2.77	2.74

*Read at the Fifth Annual Scientific Session of the American Heart Association, Portland, Oregon, July 9, 1929.

†From the Oregon State Board of Health.

MATERIAL STUDIED

To obtain a cross-section of data for study composed of patients presenting themselves in private practice and in hospital admissions the following sources were used, comprising a total of 28,661 cases, of whom 13,258 were medical patients. While these figures are all obtained from one locality in the Pacific Northwest, many of the patients came from adjacent states. To make the figures more comprehensive, figures from the larger cities of the state of Washington are desirable. The relation of cardiovascular disease to total admissions and to medical admissions is shown in Table III.

TABLE III

TOTAL ADMISSIONS		MEDICAL	CARDIOVASCULAR DISEASE		RHEUMATIC HEART DISEASE: ACUTE		RHEUMATIC HEART DISEASE: CHRONIC		GOITER	
				Per cent of medical patients		Per cent of medical patients		Per cent of medical patients		Per cent of medical patients
Private patients	5,489	5,489	1,673	30	9	0.10	125		113	8.6
Multnomah patients	3,851	1,945	1,210	62	0		325		44	
U. S. Veteran Hospital	1,003	445	151		0		0		20	
Good Samaritan Hospital	8,452	3,650	208	5	3		57		161	
St. Vincent's Hospital	8,590	1,318	230	18	4	0.11	45		479	
Doernbecher Memorial Hospital for Children	1,276	417	16		6	0.12	0		4	
Totals	28,661	13,258	3,488	26	18	0.11	552	4.9	821	6.1

The Multnomah County Hospital is the teaching hospital of the University of Oregon Medical School and is affiliated with the Out-patient Department, the Portland Free Dispensary. The patients are mostly past middle age: therefore the incidence of cardiovascular disease is high (60 per cent). Patients with chronic valvular disease are also probably more numerous than in other hospitals. The Good Samaritan and St. Vincent's hospitals are private institutions, the majority of patients being surgical (59 per cent, Good Samaritan; 86 per cent, St. Vincent's).

Of the 13, 258 medical patients, 3,488 or 26 per cent showed cardiovascular disease. Acute rheumatic fever shows a low incidence, which suggests error. In the private patient group but few children are seen, which would lower the figure, but the Doernbecher Hospital for Children shows only a slightly higher figure. Pediatricians in the Pacific Northwest are of the opinion that the disease is quite rare, though no

published studies are available. Here the incidence of acute rheumatic fever was 0.12 per cent. Climatic factors, as brought out by the authors referred to,[1, 2, 3] may be assumed to explain this, for the climate of this territory is mild.

Faulkner and White[1] found the incidence of rheumatic fever and chorea to vary from 0.2 to 5.8 per cent of medical cases. Chronic valvular disease, as seen in their study, is no criterion as to incidence, for many of these patients date their trouble to rheumatic fever in childhood. They are not natives of this part of the country. Goiter in this region is endemic. The figures take into account only goiter patients in whom circulatory symptoms were prominent.

CLASSIFICATION OF VARIOUS TYPES OF HEART DISEASE

While hospital records were found satisfactory for the above, they were disappointing for use as to structural or etiologic classification because of methods of indexing diseases. One finds such ambiguous terms as "heart failure" and "broken compensation" and "dilata-

TABLE IV

CLASSIFICATION OF VARIOUS TYPES OF HEART DISEASE OF PRIVATE PATIENTS, ETIOLOGICAL AND STRUCTURAL, TO CONFORM WITH OTHER REPORTS

CLASSIFICATION	TOTALS			PER CENT OF TOTAL CARDIOVASCULAR DISEASE
"Heart pain" group	237			
From syphilitic group		1		
Total			238	14.2
Goiter, producing cardiac symptoms	133			
With fibrillation		10		
With flutter		1		
Total			144	8.6
Rheumatic heart disease (including 5 cases of rheumatic fever, and 1 case of subacute bacterial endocarditis)	134			
With fibrillation		34		
With heart-block		1		
Total			169	10.1
Hypertensive cardiovascular disease (including 33 cases showing hypertensive menopause symptoms)	604			
Heart pain and hypertensive cardiovascular disease		227		
Auricular fibrillation and hypertensive cardiovascular disease		103		
Total			942	56.3
Syphilis of the cardiovascular system	70			4.1
Irritable heart	285			17.0
Pericarditis (including 1 case of Pick's disease)	3			0.1
Auricular fibrillation	150			8.9
Auricular flutter	3			0.1
Dextrocardia	1			0.06
Functional murmurs (congenital?)	44			2.6
Auriculoventricular block	9			0.5
Total	1,673			

tion'' with no cross index as to type of heart disease present. Nor is it possible to get accurate figures as to hypertensive cardiovascular disease for these are classified as ''arteriosclerosis,'' ''hypertension,'' ''apoplexy'' or ''hemiplegia.'' We venture to say that this condition is not peculiar to these hospitals which are all class-A institutions.

We should like to know the incidence of heart disease in surgical patients, or what percentage of elderly patients with pneumonia shows evidence of cardiovascular disease.

Records of 1,673 private patients with cardiovascular sypmptoms were studied as to etiological, structural and functional diagnoses. The results are shown in Table IV.

DISCUSSION

In the ''heart pain'' group we are aware of the difficulty of separating these into coronary occlusion, coronary sclerosis, aortitis, etc., because of confusion in differentiating them as noted by us in a former paper.[5] In all these patients, however, pain was brought on by effort and relieved by vasodilators. Electrocardiographic records were often typical, and a fair proportion were verified at autopsy. Syphilitic cardiovascular disease is not included in this group. The coronary thrombosis cases were typical, with significant history, physical findings, electrocardiograms, and, in some instances, with autopsy; 19 developed auricular fibrillation, 13 developed right bundle-branch block, and 2 right bundle-branch block with later complete block.

TABLE V

Total autopsies	465	
Goiter heart, toxic		4
Pericarditis		
Acute fibrinous		3
Adhesive, chronic		3
Purulent		3
Endocarditis		
''Malignant''		2
Subacute bacterial		2
''Rheumatic''—acute*		7
''Rheumatic''—chronic		2
Aortic stenosis		2
Coronary disease		
Thrombosis		20
Thrombosis with heart rupture		1
Hypertensive cardiovascular disease		35
Arteriosclerosis		3
Syphilis of aorta		3
Aneurysm		1
Myocarditis		
Acute toxic		2
		96

*Not acute rheumatic fever, but acute endocarditis on the basis of old rheumatic lesions of the endocordium.

In the goiter group there were 144 patients who showed various degrees of effect upon the heart. Many simple goiters were seen which are not included.

In addition to these classified cardiovascular patients, 651 patients came for heart examination in whom no heart disease was found.

Hypertensive cardiovascular disease shows a high incidence, as in other localities. This term is used to include those cases with peripheral arteriosclerosis, retinal arteriosclerosis and aortic sclerosis as shown on physical and x-ray examination rather than to attempt to separate those with slight or doubtful arteriosclerosis from those with obvious evidence of arterial thickening. It is the commonest type of circulatory disease, resulting in cardiac, renal or vascular involvement.

In 465 autopsies at the Good Samaritan Hospital 96 showed cardiovascular lesions as the cause of death. They are grouped in Table V.

CONCLUSIONS

1. Heart disease as seen in the Pacific Northwest shows a low incidence of acute rheumatic fever (0.1 per cent, while in other localities the incidence varies from 5.8 to 0.2 per cent).

2. Hypertensive cardiovascular disease is the most frequent of all types (56 per cent).

3. Goiter, being endemic, shows an incidence of 6.1 per cent of medical patients producing cardiovascular symptoms severe enough to send the patient to the physician.

4. Hospital records, though of standard type for indexing, are entirely inadequate for statistical study as to etiologic and structural diagnosis of heart disease. They are satisfactory, however, as to incidence of cardiovascular disease as compared with total medical admissions. It is hoped that studies such as this may lead to more careful supervision of hospital records by medical boards or committees of physicians who will see to it that obsolete terms are eliminated.

5. Carefully studied patients in private practice with complete records offer a satisfactory basis for statistical study but may not give a true index as to incidence in relation to total population.

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(For discussion, see page 115.)

A CASE OF SINUS ARRHYTHMIA

With Pulse Slowing, Accompanying Each Second Normal Respiration*

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INTRODUCTION

JUVENILE sinus arrhythmia, consisting of acceleration of the pulse rate during inspiration and retardation during expiration is a common physiological phenomenon. Independence of the pulse irregu-

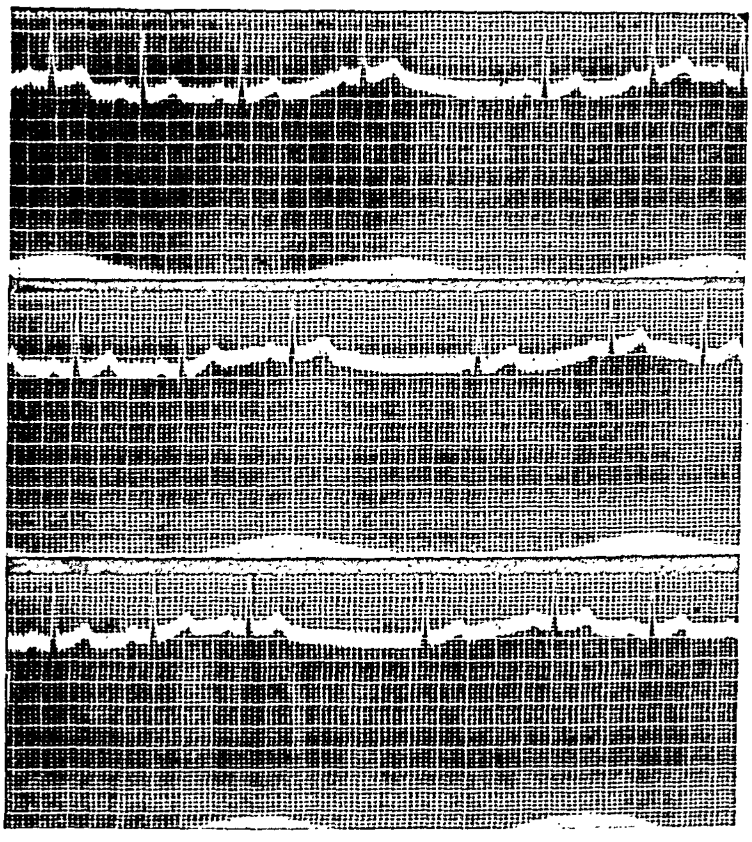

Fig. 1.—11/9/28—Continuous tracing. Normal respiration. Cardiac retardation with each second respiration. Ventricular escape.*

*The respiratory rate in all tracings was recorded on the electrocardiographic film as follows: The patient assumed a sitting position to one side of the film box, facing it. One end of a ruler was placed on his left chest anteriorly, with the other end in such a position as to cast a shadow on the film. A rise of level in the respiratory curve indicates inspiration. The method is sometimes inadequate in its representation of the depth of breathing. (cf. Fig. 6). The timing is fairly accurate. All electrocardiograms were taken in Lead II.

larity and the normal respiratory cycle is less common but has been reported frequently. Our case, showing pulse slowing with each sec-

*From the Robinette Foundation, University of Pennsylvania Hospital.

ond normal respiration, does not fit into either of these two recognized groups. To our knowledge none like it has yet been reported.

CASE REPORT

G. M., aged twenty-four years, a white male student at the University of Pennsylvania, had suffered from frequent, prolonged winter colds for many years. He had experienced mild growing pains during his childhood, but had been otherwise well. In 1925 an enlargement of his thyroid was noticed, and shortly after that time, mild dyspnea and palpitation appeared and have persisted. In February, 1928, he had an attack of bronchopneumonia and entered the Students' Ward of

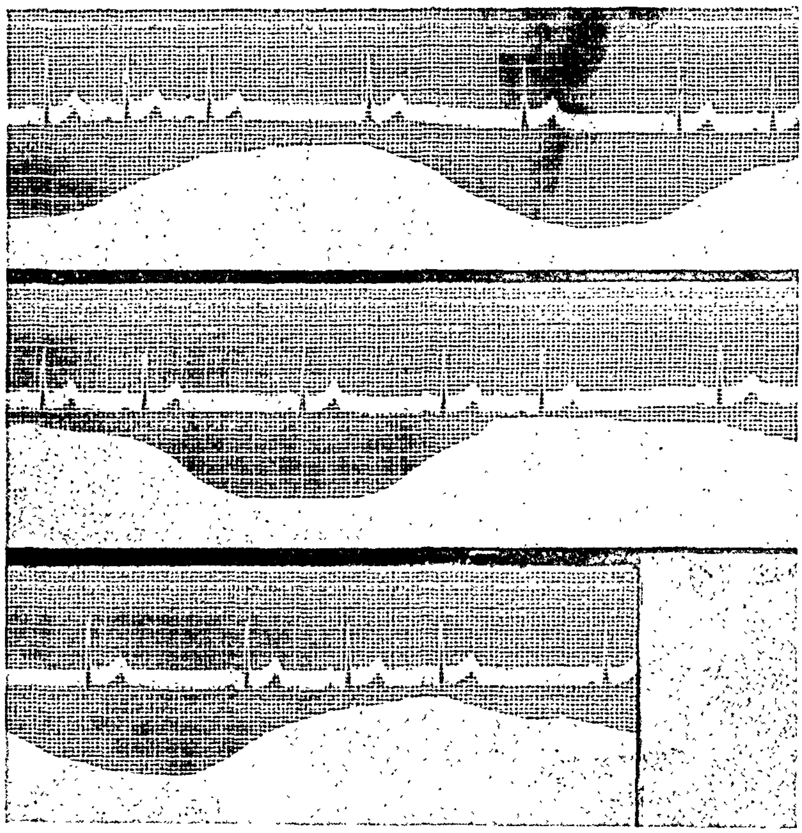

Fig. 2.—11/12/28—Continuous tracing. Deep respiration. Cardiac retardation with each respiratory cycle. Ventricular escape.

the University Hospital. During convalescence he became nervous, and on March 19, 1928, his basal metabolism was found to be plus 14 per cent. It rose in July to plus 36, and in September to plus 40. The last report of January 5, 1929 showed a basal rate of plus 24. During 1928 he gained weight.

On physical examination, the patient was found to be a powerful, well-built man. He stuttered slightly and appeared somewhat nervous. His thyroid was definitely, diffusely enlarged, but there was no thrill nor bruit. He had no tremor nor exophthalmos. By percussion, his heart was found to be slightly enlarged to the left. X-ray examination confirmed this. The sounds were of good quality without murmurs or accentuations. The blood pressure was 130/80 mm., the pulse 75, and the temperature and respirations were normal. No signs of congestion were found in the lungs, liver, or extremities.

His blood Wassermann was negative. His blood count was normal. His urine was negative. His phthalein and Mosenthal tests were normal. An x-ray of his teeth was negative, and a nose and throat examination on January 7, 1929, revealed no foci of infection.

The noteworthy finding in this patient was a marked cardiac arrhythmia in which slowing occurred with each second, or occasionally with each third normal respiration (Fig. 1). The tracing also showed ventricular escape when the heart rate was markedly retarded. During deep breathing, the cardiac slowing recurred with every respiratory cycle (Fig. 2). Ventricular escape was likewise seen. When the breath was held in deep inspiration, the heart assumed a regular rhythm and the P-waves disappeared, probably indicating a shift of the pacemaker to the junctional tissues (Fig. 3). Following this period of apnea, the 2-to-1 ratio did not reappear for some time (Fig. 4). When it did, the conditions depicted in

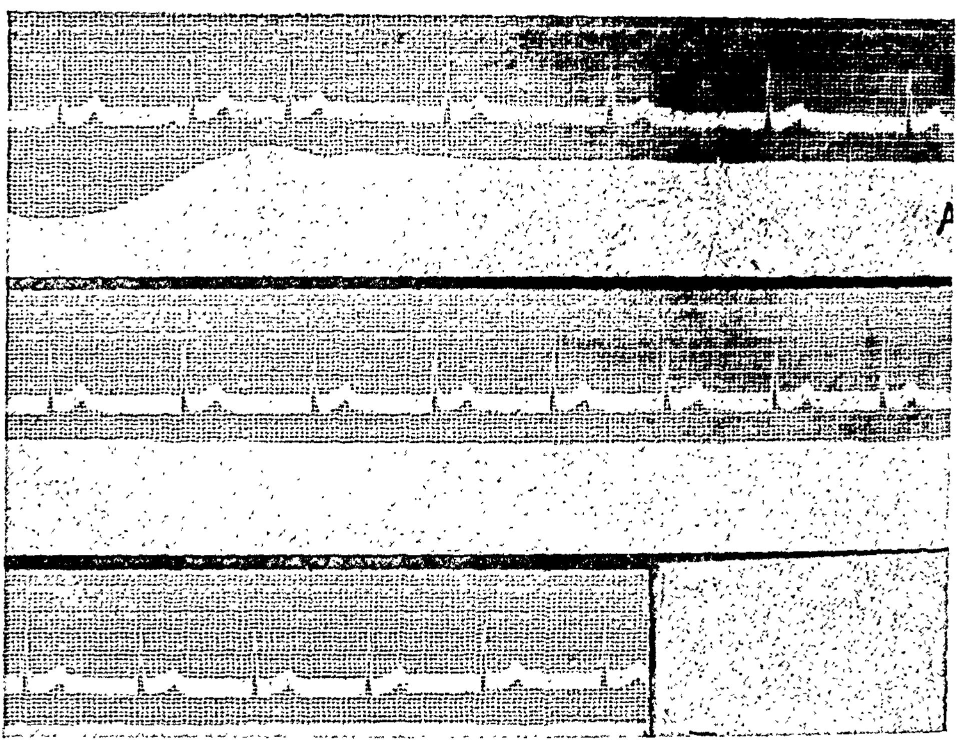

Fig. 3.—11/12/28—Continuous tracing except for the loss of ¼ inch at point marked A. Inspiratory apnea. No arrhythmia. P-waves disappear almost at once on the assumption of the expanded position of the chest.

Fig. 1 returned. After mild exertion (20 hops on the left foot), the rate rose to 140, remained at this height for three minutes, and then gradually slowed, with some irregularly recurring periods of retardation. In about five minutes the original 2-to-1 ratio was resumed. This seemed to be the normal state of affairs.

Two months later the patient returned for further study. He had his usual winter bronchitis, but no fever nor malaise. His electrocardiogram at that time showed no arrhythmia, but the heart rate had increased to 90 (Fig. 5).

Three weeks later, after he had improved but not completely recovered from his bronchitis, further tracings were made. During quiet breathing the rhythm was quite regular at a rate of 92, but during deep breathing it showed the same conditions seen in Fig. 2 (Fig. 6). During inspiratory apnea for 70 seconds it was perfectly regular with no disappearance of the P-waves, such as had been shown in Fig. 3. During expiratory apnea lasting forty seconds, the pulse at first was regular, but toward the end showed three periods of slowing (Fig. 7).

He came in once more two months after the last tracing with no further signs of his winter bronchitis. A tracing, taken at this time showed the same arrhythmia as that recorded in Fig. 1. We, therefore, consider this to be his normal state.

DISCUSSION

Sinus arrhythmia first attracted the attention of physiologists in 1860, when Ludwig suggested it to his pupil, Einbrodt, as a problem

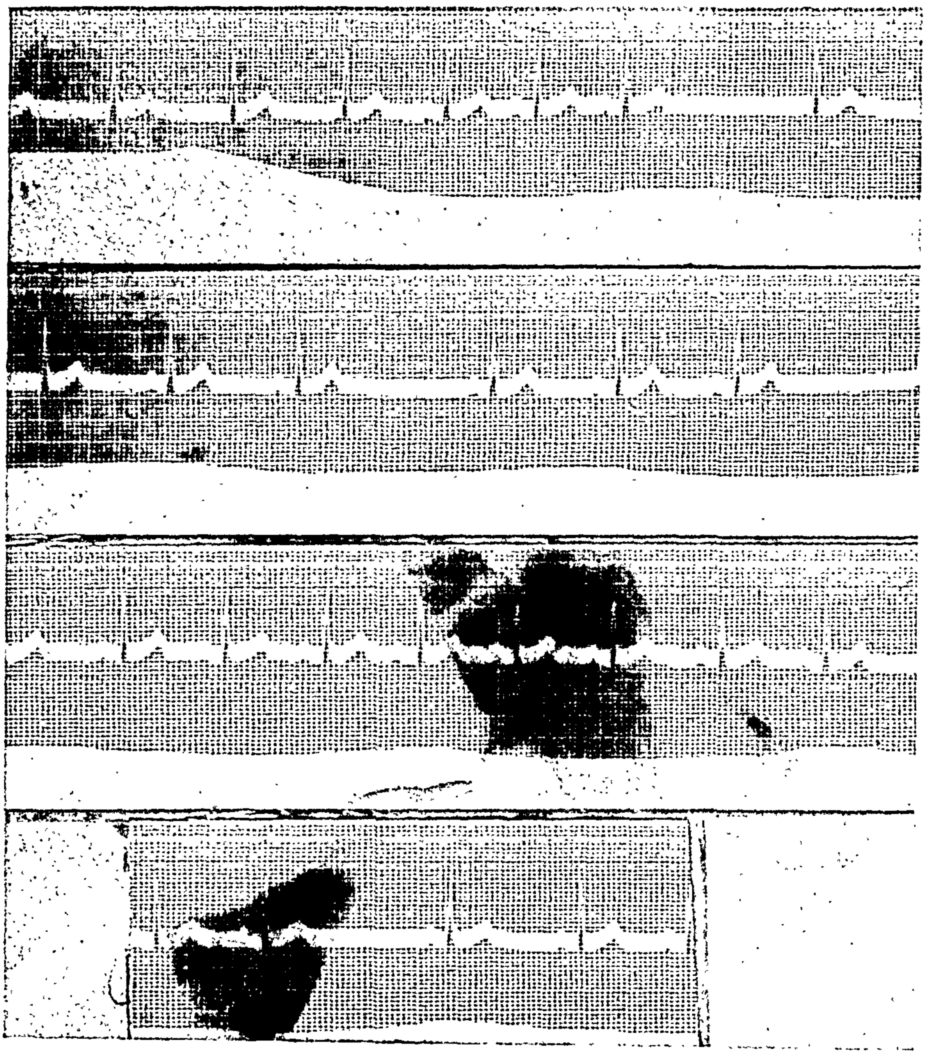

Fig. 4.—11/12/28.—Continuous tracing. Recovery period after Fig. 3. Irregular irregularity, not synchronous with respiration. P-waves appear almost at once on abandoning the inspiratory position.

for study. The earlier writers[1, 2, 3, 4, 5, 6] considered it entirely a question of alterations in the tone of the cardio-inhibitory center, because their experiments led them to believe that the accelerator system played no part in reflex regulation of the heart. Hooker[7] proved this to be an inadequate conception, in that he was able to produce reflex changes in the heart rate through the accelerator nerves after the vagi had been cut. This new knowledge, however, had little bearing

on the main disputed point, namely, the question as to the origin of the stimuli which change the tone of the cardio-regulatory centers. The hypotheses regarding this problem may be summarized as follows:

1. The stimuli arise in the lungs, due to changes in intrapulmonary pressure or in lung contour.[1, 2, 3]

2. They arise from the muscles of respiration.[5]

3. They overflow to the cardio-regulatory centers from the neighboring respiratory center, as each impulse is sent to the muscles of respiration.[6, 8]

4. They arise within the right auricle and great veins as a result of the rise of pressure within these vessels produced by the inspiratory aspiration of blood into the heart.[9, 10, 11, 12]

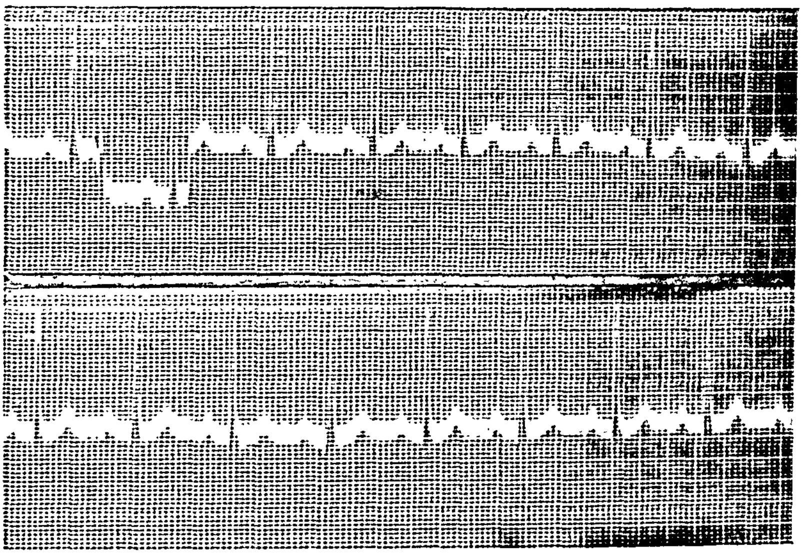

Fig. 5.—1/4/29—Continuous tracing. During bronchitis. No respiratory record. No arrythmia. Rate 90.

5. The possibility that rhythmic changes in blood P_H, due to respiration, can be the cause of sinus arrhythmia has been suggested by Sanderson,[13] but does not agree with our present knowledge of the subject.[14]

On account of its general characteristics and its behavior under the conditions imposed, the irregularity in our case almost undoubtedly belongs in the group generally known as "vagal" or "sinus" arrhythmias.* It differs, however, from the common juvenile type. The normal "youthful arrhythmia" (Mackenzie) seems dependent as a rule upon changes in either direction from what might be considered the basal rate of the heart, quickening during inspiration and slowing during expiration. If either of these is more pronounced, it is usually the former. Our patient's arrhythmia, however, seems almost entirely

*An additional bit of evidence, the effect of atropine was not studied, because the patient preferred not to have the drug administered, and because it was not thought necessary, since any type of tachycardia abolished the irregularity.

dependent upon a periodic slowing, usually during expiration, with very little, if any, inspiratory acceleration above what might be considered the basal rate of his heart. This fact is most definitely shown in Fig. 6.

Wedd[15] believes that this general class of arrhythmias is due to an imbalance between accelerator and vagus control of the heart, with periodic increased activity of the weaker of the two systems in an

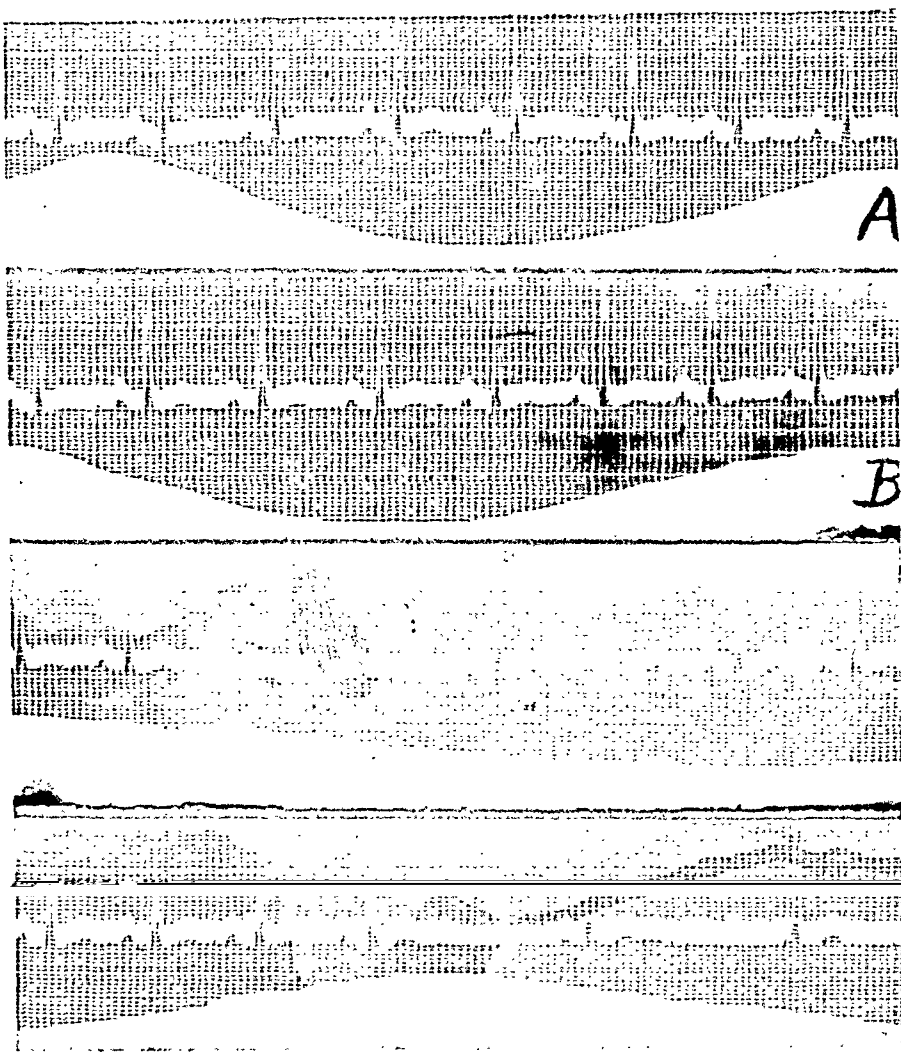

Fig. 6.—1/29/29—Continuous tracing. Toward the end of attack of bronchitis. Two normal respirations followed by two deep respirations. The respiratory record does not show accurately the depth of respiration. *A* shows the last normal breath. *B*, the first deep breath. No arrythmia with normal breathing. Arrythmia occurs during deep breathing.

attempt to bring about a more perfect balance. In the light of this hypothesis, our patient might be thought of as a case of sympathetic preponderance, possibly ascribable to his thyroid disease. The vagus, being the weaker of the two systems, periodically attempts to equalize the balance, but has greater difficulty in doing so during any period

of increased cardiac activity, such as that accompanying the attack of bronchitis (Figs. 5 and 6).

Wedd did not discuss the mechanism underlying this periodic vagus intensification, nor can we offer an adequate explanation for it in our patient. However, the following facts are brought out in our tracings. During inspiratory apnea the P-waves disappeared from the electrocardiogram. Their disappearance and reappearance followed quite closely upon the assumption and abandonment of the expanded position of the chest (Figs. 3 and 4). It is therefore possible, in our patient, that the inspiratory position stimulates the vagus, inhibiting the

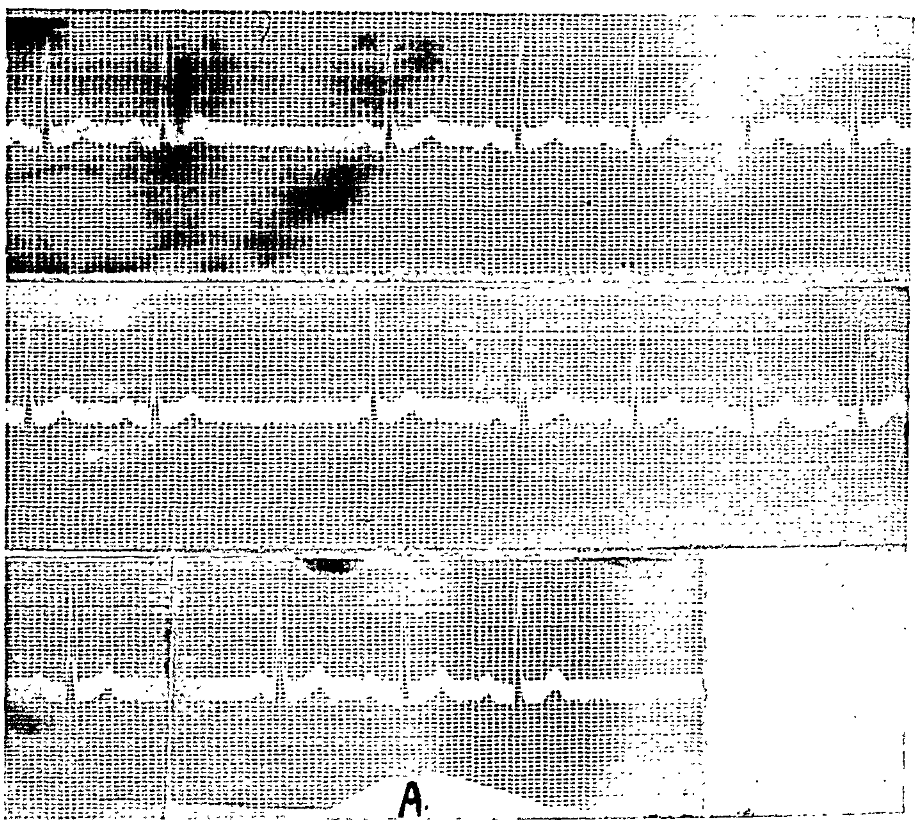

Fig. 7.—1/29/29—Continuous tracing. Toward the end of expiratory apnea. The respiratory curve does not show during apnea, but the resumption of respiration may be seen at *A*. Three periods of cardiac retardation in the absence of respiration.

sino-auricular node, thereby causing a shift of the pacemaker to the junctional tissues. If this is conceded, periodic vagal stimulation as a result of rhythmic assumption of the inspiratory position might be the factor causing the arrhythmia during respiration. The resulting inhibition, after a short latent period, appears during expiration. This latent period is shown in Figs. 3 and 4, at the beginning and at the end of inspiratory apnea.

The occurrence of the arrhythmia during expiratory apnea, however, necessitates the postulation of another source of stimuli, presumably extrathoracic, affecting the vagus center, when rhythmic stimuli from

the thorax cease. This may be some point in the central nervous system, as suggested by Fredericq.[6] Anoxemia, the result of apnea, which is known to increase cardio-inhibitory tone[14, 21, 22] may aid this secondary source of stimuli in producing its effect. During inspiratory apnea, the action of this subsidiary source of stimuli was prevented from becoming apparent, possibly because continuous vagal stimulation overshadowed it.

The 2-to-1 relation of cardiac arrhythmia and respiration is the most unusual and inexplicable feature of this case. Vagal arrhythmias independent of the normal respiratory cycle are seen fairly frequently.[16, 17, 19, 20] They occur as a rule in older people, but may appear in the young. According to Lewis[17] they usually become synchronous with the respiratory cycle when breathing is deepened. However, no case has been found in the literature similar to the one reported here. It suggests as its cause some cumulative factor, not strong enough to become effective with each quiet respiration. It was not due to change in the depth of alternate respirations since this was not present. It recurs too regularly for it to be the accidental coincidence of a periodic nonrespiratory cardiac retardation with each second respiratory cycle.

SUMMARY

A case is reported in which a hitherto undescribed form of cardiac arrhythmia appears. Under normal respiratory conditions retardation of the heart occurs with each second respiration. Simultaneous electrocardiographic and respiratory tracings are shown, and a discussion of the mechanism involved is presented.

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ELECTROCARDIOGRAPHIC ELECTRODES*

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Columbus, Ohio

THE most disturbing factor encountered by one doing technical electrocardiography is the proper application of electrodes and the resulting overshooting. Since the more or less universal abandonment of the solution electrode, there have been numerable types recommended, such as plates of various metals and the direct application of copper wire. These all require preparation of the skin before application, by heat, salt solution, acetone, scrubbing, etc., so as to reduce overshooting to a minimum.

In order to reduce overshooting, I have for the past six months used a pad known as "The Chore Boy," manufactured by the Metal Textile Corporation, Orange, N. J., made primarily for scouring kitchen utensils. This pad has woven

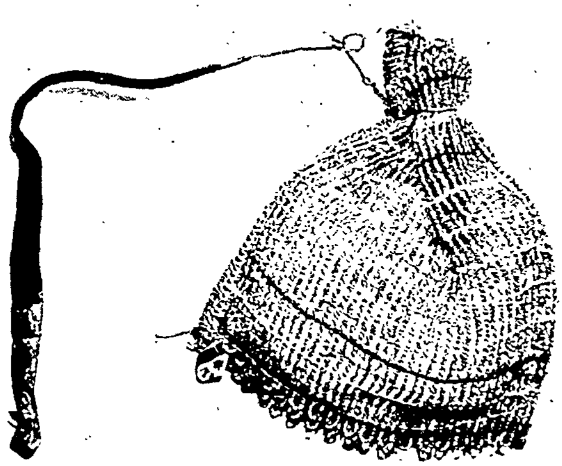

Fig. 1.—The pad prepared as an electrode.

through its loose mesh, fine strands of copper wire which are rough and resemble long turnings or shavings. The pad is made in the form of a mitt, having an opening at one end, by which it is filled with a small amount of cotton. This opened end is brought together and bound by a copper wire, which by an ordinary radio ground connection is connected with the lead wires of the electrocardiograph.

The pads are saturated with salt and moistened with hot water. Two of these are placed on the arms of a comfortable chair, while the third is placed on a rubber mat insulating it from the floor. The patient is required to remove the left shoe and stocking, preparation of the skin is unnecessary. The left foot and the palms of the hands are placed on their respective pads. Numerous electrocardiograms can be taken without rewetting the pads, but if the skin resistance is high, salt and water is again poured on the pads. The patient should be told to relax and be as quiet as possible.

Occasionally, somatic tremors or a traveling string is encountered. On these rare occasions the pads for Leads I and II are held to the wrist by rubber bands,

*From the Cardiological Departments of White Cross and Children's Hospitals.

made by cross sectioning an ordinary automobile inner tube. By this method overshooting has been completely overcome. It is probably due to the fact that the rough strands of copper shavings press deeply into the skin and make a more perfect contact than any other type of electrodes now available.

CONCLUSIONS

1. The use of these copper woven pads removes the necessity of skin preparation.
2. The electrodes are constantly in position and need not be connected for each electrocardiogram.
3. Overshooting has not been encountered, and standarization of the string is made easy by using this method.

Society Transactions

AMERICAN HEART ASSOCIATION

FIFTH ANNUAL SCIENTIFIC SESSION

JULY 9, 1929

The fifth annual scientific session of the American Heart Association was held in the auditorium of the Woman's Club, Portland, Oregon, July 9, 1929. The session was called to order at 2:10 o'clock by the president, Dr. William H. Robey of Boston, Mass.

DR. WILLIAM H. ROBEY.—Will the fifth annual meeting of the American Heart Association please come to order. Dr. Herrick has been upset because, owing to a change in the time of his clinic, he felt he could not come to this meeting. We regret that he cannot be here for the whole session, but as he is here now, we will ask him to try his lecture on us.

1. DR. JAMES B. HERRICK, Chicago, Ill.—**Coronary Occluson.** (For original article see AM. HEART J. 4: 633, 1929.)
2. DR. T. HOMER COFFEN, Portland, Ore.—**The Incidence of Heart Disease in the Pacific Northwest.** (For original article, see page 99.)
3. DR. J. H. CANNON, Charleston, S. C.—**Clinical Observations on Syphilitic Occlusion of the Coronaries.** (For original article, see page 93.)
4. DR. IRVING R. JUSTER and DR. HAROLD E. B. PARDEE, New York, N. Y.—**An Electrocardiographic Study of Fifty Cases of Cardiovascular Syphilis.** (For original article, see page 84.)
5. DR. EUGENE S. KILGORE, San Francisco, Cal.—**The Problem of the Nervous Heart.** (For original article, see page 9.)
6. DR. ROBERT L. BENSON, Portland, Ore.—Exhibits of specimens of rupture of the heart due to cardiac syphilis in the Scientific Exhibit of the American Medical Association.

DISCUSSION

DR. WILLIAM H. ROBEY, Boston, Mass.—I want to say a word about Dr. Herrick's interesting paper. I think in cases with repeated attacks of cardiac pain small areas of scar tissue are found at autopsy resulting from occlusion of twigs of the coronary. That has been shown by Louis Gross and others. Occlusion of twigs is probably the cause of the attacks of angina pectoris, and they have also shown how one side by anastomosis will help the affected side of the heart.

I want to emphasize other symptoms replacing pain. I recently saw a man weighing 230 pounds who had always been perfectly well, but who had dyspnea in very much the way pain comes in angina pectoris. Walking along the street this patient could go only about a block when he would be forced to stop because of intense dyspnea. He has been given cardiac rest, the symptom has entirely disappeared, and he is able to walk without attacks of dyspnea.

Another important symptom is *nocturnal dyspnea.* A person may be free of symptoms throughout the day, yet during sleep when the heart quiets down there is a deficient blood supply to the muscle with a resulting anoxemia and the patient wakens with dyspnea. A prominent man in Boston went to a colleague of mine for a thorough examination. He was planning an extensive trip and was told that it was safe to take it, but he collapsed on the train, was examined at the Mayo Clinic and advised to return to Boston where he died three weeks after his arrival.

Now the doctor who made the first examination was a very careful man, but he had forgotten to ask about nocturnal dyspnea. This patient, once or twice a night for a year, had been wakened by air hunger, but he and his wife had neglected to say anything about it, and because the doctor had not thought to ask, a very interesting point had been overlooked.

In the milder cases of coronary disease, time and rest may establish the *function of the thebesian vessels, thus furnishing an increased blood supply to* the impoverished muscle.

As to the pain of coronary disease, it seems to me it must be within the heart muscle. Of course, we do not know just how the pain is produced, but I think there are certain reasons against the theory of the French school and also of Dr. Allbutt. I have always believed (as maintained by Mackenzie and others) that it is a spasm of the heart vessels, because there is an analogous pain in the muscles of the leg. A patient with arteriosclerosis is suddenly seized with pain in the leg; he rests a moment and the pain ceases. That was probably a spasm of the leg vessels, the muscles calling for more blood.

We have studied at the Boston City Hospital cases of gall bladder disease in which there has been a question of angina pectoris. In certain cases where there has been great doubt, we have recommended operation and have found that gall bladder disease did exist. It seems to me if there is any great doubt in a chronic case it is better to give the patient the benefit of operation. One man who was under my care for a number of years had shortness of breath and substernal oppression when walking from his office to his house, which necessitated his climbing a small hill. He had more or less indigestion at the same time and finally had a mild attack of jaundice. He was operated on and found to have a small, narrowed gall bladder. He recovered from the operation very well, but about eight weeks later had a hemiplegia with complete aphasia. About four months later he had a very definite attack of coronary occlusion with cyanosis, sweating and fever, and died in a few hours.

DR. GEORGE DOCK, Pasadena, Cal.—In regard to the matter of pain confusing other conditions, one of the best cases of left coronary occlusion I ever had was a doctor about 50 years old whom I saw when he was well and strong, but who had had this pain for some time, with dyspnea on exertion. To me his condition was perfectly clear, but he, an unusually keen and clear-minded country practitioner, insisted that he had cancer of the stomach. That was what he came to me for. We often discussed it in the time I saw him, and he insisted that his pain was exactly like that of cancer of the pylorus. It turned out, however, that he did not have cancer, but an obstructed left coronary.

Cases of syphilitic disease of the coronary are certainly among the most interesting of all. In many cases we have no doubt about the etiology. The most extraordinary one I ever saw was in a man 50 years old, who was brought into the hospital at Ann Arbor with advanced decompensation of long standing, and who died there. He was a very intelligent man and had some intelligent relatives with him who knew his history. At the age of twenty years he had a chancre followed by a period of anginal pain. The attacks were among

the most characteristic I have heard described, but while most patients with angina are obliged to keep still during the attacks, this young man, who had an ungovernable temper, when the attacks began would run around the room cursing and screaming, showing about as much muscular activity as a man in good health. He got over that attack, remained free from symptoms for a long time, but finally developed decompensation and died. Post-mortem examination showed that he had a healed infarct about 3 cm. in diameter, evidently of long standing. There were two features of interest in his case—the strangeness of his attacks of pain, and the fact that having had a severe lesion like that he recovered so completely. Of course that is not unique, but I thought at a meeting of this kind it might be worth while to add it to the comments that have been made.

DR. WALTER J. WILSON, Detroit, Mich.—Recently I had a case of *angina sine dolore* in a young man of 26 years, the presenting symptom being tachycardia, the auscultatory rate being 175, but on electrocardiographic examination we discovered a case of ventricular tachycardia and the rate 300. There was a leucocytosis of 31,200. There were no signs of decompensation. Under treatment of digitalis he improved, and the rate became normal in eight days, but when last seen he had right bundle-branch block. The use of quinidine was ineffective and the symptoms unpleasant.

I think that in many of these cases, emphasis should be laid on electrocardiographic examination, which, in the vast majority of cases, will elucidate the case.

Within the last few months, I have seen a young negro 18 years old, who at 14 years developed syphilis from venereal contact and now has a marked aortic insufficiency. In some cases, years do not have to elapse before sufficient damage is done to the aortic valve to cause insufficiency.

DR. B. O. RAULSTON, Los Angeles, Cal.—This seems a proper time to call attention to a report made by Dr. Fitz of Boston of a case, a woman of middle age, a school-teacher, who had clinically a typical angina, and who in the course of a study to determine whether or not she might have disease of the gall bladder was given iodides intravenously. She developed the classical symptoms of coronary occlusion and died. Another thing that is somewhat surprising is that we do not hear anything about the possible effect of thrombosis of the small twigs of the coronary producing acute changes and then chronic changes that may account for many of the irregularities of the heart. A good deal of work has been done on that subject in France and England, and I feel that this may be the true basis for irregularities which we attempt to explain on other grounds.

DR. LESLIE T. GAGER, Washington, D. C.—The embolic phenomena of coronary thrombosis—those which we have been accustomed to call embolic, and which Dr. Herrick suggests may be due to thrombosis in situ—are of increasing interest. I should like to cast my opinion in favor of the embolic theory, for the reason that in a number of carefully studied patients I have found no evidence of infection, either local or general. In one of the most recent patients, a man of 56 years, who had had a coronary thrombosis eighteen months previously, the first symptom was pain in the right arm which lasted a few minutes. Two weeks later during the journey to the hospital he had pain in the right leg lasting several hours. During this attack he had no fever, and his leucocytes on admission were 7000. Subsequently he had pain in the lower abdomen, without fever, for three days, next a cerebral accident with a left hemiplegia. This was not accompanied by fever and also cleared up in the course of several days. Then after another week—this was six weeks after the initial pain in the arm—he had severe, agonizing pain in the upper abdomen, began to vomit dark red blood, and died

after twenty-four hours. The post-mortem findings confirmed the clinical diagnosis of coronary thrombosis with a mural infarct in the left ventricle, and hemorrhagic infarction of the entire ileum. In the colon there was evidence of regression of an area of hemorrhagic infarction which was considered the cause of the lower abdominal pain two weeks before death. In the brain no evidence in the right cerebral vessels could be found to account for the hemiplegia on the left side. In other words, a series of accidents had occurred, which in the arm and leg in the brain left no traces; in the large intestine, changes which were resolving, and in the small intestine, the acute terminal phenomenon of arterial occlusion. The embolic theory, with multiple fragments being cast off at intervals from the intracardiac thrombus, would better fit the facts in such a case, it seems to me, than the assumption of thromboses in these several sites.

DR. ROBEY.—I am glad to have Dr. Wilson speak of tachycardia. I think it is quite as important a symptom as dyspnea or pain. I have recently seen a physician of 62 years who had attacks of paroxysmal tachycardia. The physical examination was not important, but an electrocardiogram taken after the third attack showed a downward deflection of T_1 and T_2 with concavity of the S-T interval. This we find in cases of coronary thrombosis, and I made that diagnosis notwithstanding the absence of pain. Fred Smith found that after ligation of a coronary branch in dogs a similar electrocardiogram was obtained, but in a few months there was a return to a normal T. An electrocardiogram of my patient taken several months later was similar to the first.

DR. GAGER.—The early diagnosis of cardiovascular syphilis is a problem which is of great importance to all of us. On the Atlantic seaboard, as rheumatic fever declines in incidence going from north southward, syphilitic heart disease and hypertensive-arteriosclerotic heart disease increase. The differential diagnosis of these two types is often exceedingly difficult; therefor, if we can find in the electrocardiogram definite evidence of syphilitic myocardial involvement, it is an extremely valuable aid. Personally I have had a great deal of difficulty clinically and with the electrocardiogram in making this differentiation. For example, I have recently seen a patient in whom a six-foot plate showed dilatation of the aorta, so well demarcated that the roentgenologist was willing to make a diagnosis of aneurysm. At post-mortem, however, the lesions were apparently entirely arteriosclerotic. In other patients with undoubted clinical syphilis, there have been seen those changes which Dr. Juster has shown in the T-wave. I am thinking of a patient I saw a week ago in whom necropsy showed, in addition to aortitis and aortic insufficiency, patent coronary orifices, extensive fibrosis of the myocardium, coronary sclerosis with areas of thrombosis. In such cases the electrocardiographic evidence so far has seemed to be on the side of arteriosclerotic heart disease without respect to any specific etiology or to pathognomonic structural changes.

DR. AUDLEY O. SANDERS, Palo Alto, Cal.—Dr. Juster's paper has brought to mind a problem that came to our group a few weeks ago. A young man came to us having had a diagnosis of syphilis and giving a history of a four-plus Wassermann in 1923. Later Wassermanns, both blood and spinal fluid, had been negative. The patient denied luetic infection. Our blood and spinal fluid examinations were negative. The electrocardiogram was not definitely abnormal. The x-ray, however, showed a very marked dilatation of the ascending aorta. With this and the questionable history of lues we were inclined to a diagnosis of luetic aortitis with dilatation. This patient had another condition which led to his death. At autopsy we found, to our surprise, no evidence of luetic aortitis but a constriction of the arch of the aorta with marked dilatation of the ascending aorta proximal to that point. The autopsy diagnosis was that of a congenital condition of the aorta.

DR. JUSTER (closing).—This observation of the abnormality of the T-wave was made four years ago. Of course it took quite a while to collect these cases, but we have found that we could always use it as a diagnostic point. Quite often you see a patient in the thirties with aortic insufficiency with a positive Wassermann and a history of rheumatism, and the question arises—is the etiology syphilis or rheumatic fever? By using this method of the inversion of the T-wave, provided no digitalis has been given, we have been able to secure great help in the diagnosis of syphilitic aortic insufficiency. In watching some of these cases develop this inversion, increasing severity of symptoms was noted. In view of the fact that the T-wave inversion is common in valvular cases, repeated electrocardiograms may be an aid in determining whether or not our treatment of early syphilis will prevent the development of the cardiovascular lesion. We know we get a definite result in early lues, but we have not followed these cases long enough to say whether we have prevented the development of cardiovascular disease. The cases that develop the T-wave inversion do very poorly, and of course the ultimate outcome is usually fatal. We find that treatment after this T-wave abnormality has occurred is of no help whatever.

Department of Reviews and Abstracts

Selected Abstracts

Lightwood, R. C., and Davies, M. Llewelyn: A Clinical Study of Acute Rheumatism. Brit. M. J. 495, September 14, 1929.

This report is based on work at the Rheumatism Supervision Center, Royal Borough of Kensington. The primary object of this is to prevent relapses and to care for those children whose hearts are already involved. In the latter group of children these two objects are inseparable. The functions of the rheumatism supervisory center as outlined should be: first, to make use of all the measures available for preventing relapses in rheumatic children, and second, to supervise the after care of children already the victims of rheumatic heart disease.

The lines on which recurrences of rheumatism may best be prevented are: one, correction of unsuitable environmental conditions; two, attention to general health; three, treatment of diseased tonsils; four, education of the parent in the correct management of the rheumatic child.

Hill, N. Gray, and Allan, Mary: The Rheumatic Type. Brit. M. J. 499, September 14, 1929.

A general study of 562 rheumatic children and 536 other patients under similar conditions admitted to the hospital for study leads to the conclusion that there is no type as regards complexion, color of hair, eyes, etc., that can fairly be described as the rheumatic type of child. The total division of complexion is about equal between fair and dark children. There also was no evidence that the skin of the children of the rheumatic group was more dry than among the nonrheumatic patients.

White, Paul D., and Mudd, Seeley G.: Observations on the Effect of Various Factors on the Duration of the Electrical Systole of the Heart as Indicated by the Length of the Q-T Interval of the Electrocardiogram. J. Clin. Investigation 7: 387, 1929.

A study is here reported of the measurements of the Q-T interval made on carefully selected electrocardiographic plates with the help of the Lucas comparator in 213 individuals, of whom 50 were normal to act as controls and 163 were abnormal subjects to illustrate the effect of various pathological conditions. The prime factor influencing the duration of both mechanical systole and the Q-T interval of the electrocardiogram has been found to be the heart rate. The faster the rate, the shorter the duration of the Q-T interval, although at faster rates the relative proportion of the heart cycle made up by systole steadily increases.

The measurement of the duration of the Q-T interval of the electrocardiogram is apparently of little or no clinical value from the study of these cases.

Gray, S. H., and Aitken, Louis: Late Gross Lesions in the Aorta and Pulmonary Artery Following Rheumatic Fever. Arch. Path. 8: 451, 1929.

It is the purpose of this paper to report the late gross lesions that were discovered in the aorta and pulmonary artery of the rheumatic hearts examined in four patients. In one of these there was an aneurysm of the aorta in which all

the evidence pointed to a rheumatic origin. The criteria of Pappenheimer and von Glahn for the establishment of the diagnosis of rheumatic fever has been adopted in selecting cases for the study. All four patients were adults, ranging in age from 20 to 47 years of age. The late lesions persisted in scarring of the media and thickening of the intima.

The authors believe that the gross lesions occur as a result of a confluence in a localized area of the small flame-shaped scars occurring during the acute stages of the disease. It was possible in each instance to determine that syphilis had not been present.

The formation of aneurysm appears to be the result of a break in the aorta with a subsequent dissection of the aorta along the lower part of the media.

Small, James Craig: The Rôle of Streptococci in the Rheumatic Diseases. J. Lab. & Clin. Med. 14: 1144, 1929.

The rôle of streptococcus in rheumatic disease is discussed and a hypothesis embracing a dual nature of its pathogenesis is offered as follows:

The specific toxin of a streptococcus is suggested as operative in the production of the "destructive" and "proliferative" types of lesions in rheumatic fever, while the patient's hypersensitization to an allergen associated with the protein of streptococci is presented as concerned in producing the "exudative" lesions. The specificity of this sensitizing substance or allergen is not dependent upon the type of streptococcus supplying it.

Three types of reaction in patients are described as "exudative lesions" best exemplified by the acute arthritis; the "proliferative" lesions typified in their purest form in the subacute progressive cardiac lesions in the heart; and the "destructive" lesions best seen in the heart muscles of patients who have died early in an attack of rheumatic fever attended by an overwhelming clinical toxemia. This lesion amounts to actual sterile necrosis of the muscle fibers occurring in areas of a considerable extent.

The author believes that the destructive lesion is brought about by high concentrations of a specific endotoxin derived from a particular group of streptococci; the proliferative lesion because of a stimulating effect of weaker concentrations. The exudative lesion appears when the patients begin to develop immunity to the specific toxic factor and is brought about by the establishment of a condition of hypersensitiveness which is a manifestaiton of the Arthus phenomenon. These lesions may be accounted for on the basis of bacterial "protein" specificity and not on the basis of bacterial group or type specificity.

The author proceeds to describe chronic arthritis as an allergic disease, the hypersensitive state of the patient being due to this allergen contained in streptococci without regard to a particular type.

Levine, Samuel A., and Brown, Charles L.: Coronary Thrombosis: Its Various Clinical Features. Medicine 8: 245, 1929.

The author makes the following considerations as the result of an analysis of the clinical features of 145 cases of coronary thrombosis and the pathological data of 46 of these.

1. Angina pectoris generally precedes attacks of coronary thrombosis but there were a few instances in which it was quite clear that the patients not only had no angina but no evidence of any important preexisting disease could be made out.

2. Coronary thrombosis frequently developed in long standing mild diabetics, but because the age incidence was the same in diabetic as in nondiabetics it would seem that the diabetes merely indicated the type of individual who would develop coronary disease rather than that it had any causative relation to it.

3. Hypertension was present in the great majority of cases but in some it was quite definitely known that the blood pressure was normal before the attack. Arteriosclerosis was a very variable finding. In some it was strikingly limited to the coronary arteries.

4. Syphilis was found to be a very rare cause of coronary thrombosis, and other infectious diseases seemed to have very little etiological significance.

5. Hereditary factors, although extremely difficult to analyze, were found to be most important especially in those patients having coronary thrombosis at a comparatively young age. Possibly as a part of the hereditary factor there seems to be a certain physical type of individual who is more apt to develop this disease. The type is that of a well set and strong individual, somewhat overweight, whose limbs and especially the forearms are round rather than flat. He generally has been quite active physically, either in sport or at work.

6. The average age in this series was 57.8 years. There were 111 males and 34 females. The marked disproportion in the sexes cannot be easily explained but brings up the possible relationship of physical work and tobacco to coronary disease, both of which factors are more prominent in the male than in the female.

7. The typical clinical picture of acute coronary thrombosis was discussed in detail. In addition certain atypical features were emphasized that are commonly overlooked and which are important in making a proper diagnosis. The pain was found to vary from a slight discomfort in the chest to the most terrific agony, and varies in the location from the upper abdomen to the upper sternum and throat. There were *not infrequent cases that were entirely painless.* It was emphasized that in some instances the entire picture resembles very closely an acute surgical abdomen. Although there customarily was a fall in the blood pressure with the attack, in some instances this did not occur.

Fever and leucocytosis developed early in most cases but there were rare exceptions. The temperatures must be taken rectally as the mouth readings were frequently normal when an actual fever was present. The important features on examination were the appearance of shock, the distant heart sounds, gallop rhythm, the development of various irregularities in the rhythm of the heart, occasionally a pericardial friction rub, râles in the lungs and sometimes an engorgement of the liver.

Certain changes in the electrocardiograms were found to be invaluable as aids in diagnosis, both during the early days and also in the later weeks following the attack. Besides those electrocardiographic changes that have previously been described, attention was called to the development of a prominent Q wave in Lead III in many of these cases.

The urine was frequently found to contain sugar and evidence of renal damage such as albumin and casts. At times there was marked oliguria or a suppression of urine. These findings generally were transient.

Both the types of death and the types of recovery, because of their variability, were analyzed and for the most part they were found to fall into fairly definite groups. This enabled one to predict somewhat more clearly the course of the disease.

8. The important conditions that at times had to be considered in differential diagnosis were an acute surgical condition of the abdomen, angina pectoris, pneumonia, diabetic acidosis, and finally so-called chronic myocarditis. The proper diagnosis in most cases is possible, although to make it in some, all our methods of study including electrocardiograms may be necessary.

9. The criteria for prognosis in individual cases were found to be most unsatisfactory. In general about 50 per cent have an immediate recovery. No single feature seemed to be reliable as indicative of a good or poor prognosis. Apparently mild cases occasionally died and very severe ones recovered. Slight differences in the mortality were found when certain factors were analyzed such as age, sex, the

development of pericarditis, and auricular fibrillation. Ventricular tachycardia and heart block seemed to have a greater mortality than the average. Even the type of change in the electrocardiogram had no influence on whether the patient would recover or not.

10. The question of treatment for the present must be based partly on theoretical grounds as there are no data available to compare the end-results of one régime with those of another. The acute and rapid character of the disease often makes our deductions as to therapy fallacious, because frequently many drugs are given in a short time and it is difficult intelligently to appraise the proper value of any single one. A proper understanding of the pathological process going on during coronary thrombosis will help to some extent in rationalizing our therapy. Certain features in treatment were discussed which we consider may prove life saving in occasional cases.

11. A careful pathological study of 46 of these cases was made. Apart from the ordinary findings some interesting correlations with the clinical features were uncovered. It was found that not infrequently a thrombus formed in the right ventricle as well as in the left as a result of a thrombosis of the left coronary artery. This happened when the interventricular septum was involved. There were two painless cases in which the right coronary artery was thrombosed. In nine cases rupture of the ventricle occurred. The most frequent artery involved was the left descending coronary and the favorite site of the thrombus formation was about 2 cm. below the bifurcation with the left circumflex coronary artery.

Stewart, Harold J.: The Effect of Exercise on the Size of Normal Hearts and of Enlarged Hearts of Dogs. J. Clin. Investigation 7: 339, 1929.

The authors have investigated this subject, using dogs in which defects of the mitral valve have been made by operation and in which enlarged hearts have in consequence developed. There were no signs, however, of heart failure. Control animals were included in the study. The dogs had been the subjects of other experiments and had been operated on two to three and one-half years ago.

The dogs were first trained to run on a treadmill and after preliminary training the effect of running on the size of the heart was investigated by means of x-ray photographs of the heart. The dogs were allowed to run only as long as they did so voluntarily usually from twenty-five to sixty minutes. It was found on examining the x-ray photographs that the size of both normal and enlarged hearts always decreased. There was no evidence of dilatation of the heart. The heart muscle of these animals is presumably free of myocardial disease since no infection had been introduced in the experimental conditions. These observations bear out the general assumption that myocardial disease is necessary for the development of heart strain, dilatation and cardiac collapse.

Boas, Ernst P., and Weiss, Morris M.: Heart Rate During Sleep as Determined by the Cardiotachometer. J. A. M. A. 92: 2162, 1929.

By means of the cardiotachometer, the authors have observed the pulse rate over long periods of time during sleep, rest and activity, in both normal and abnormal human subjects. This study has shown the tremendous variability of the normal heart rate as well as its marked reduction and relative stability during sleep.

They have also noted in patients with exophthalmic goiter active myocarditis and at times mitral stenosis that the drop in rate during sleep is greatly diminished. They point out that this increased rate during sleep may serve as a valuable aid in diagnosis especially in differentiating organic heart disease from those patients with a neurogenic tachycardia.

Hart, A. P., and Silverthorne, L. N.: A Case of Acute Bacterial Endocarditis. Canad. M. A. J. 21: 305, 1929.

A case of bacterial endocarditis is reported embodying some extremely interesting findings in a female child thirteen years of age. Encephalitic symptoms were the outstanding features in the case when the child was admitted to the hospital. Streptococcus viridans was recovered from the culture of the spinal fluid. Petechial hemorrhages, palpable spleen, enlargement of the heart with a systolic murmur and the recovery from the blood of streptococcus viridans were the main clinical findings. Autopsy revealed petechial hemorrhages in the heart, brain, skin and mucous membranes with embolic manifestations in the heart and brain.

The patient had had measles, scarlet fever and whooping cough and two attacks of rheumatic fever in the last two years of her life. Because of the attacks of rheumatism, she had been kept at home though apparently well. There were no evidences of rheumatic carditis at autopsy. The valves were thickened and there were fresh vegetations on the margin. Microscopically the picture of the heart as a whole was that of bacterial endocarditis engrafted on an old rheumatic condition.

Hanzlik, P. J., and Wood, D. A.: The Mechanism of Digitalis-Emesis in Pigeons. Jour. Pharmacol. & Exper. Therap. 37: 67, 1929.

The emesis of digitalis has been studied in pigeons with the view of determining the seat of action by physiological and pharmacological methods and also according to the distribution of the drug in the body. The results obtained on pigeons indicate that the seat of emesis is peripheral in origin, the action consisting predominately of a vagus-reflex mediated through the local irritant action of the digitalis concentrated in the liver, other abdominal viscera not being excluded. The seat of emesis is not in the heart. It also seems that the seat of emesis is peripheral in origin and not central.

The following results support these conclusions: Digitalis is chiefly concentrated in the liver as compared with the blood, heart and lungs and the liver shows a comparatively greater sensitivity to digitalis than the peritoneum. Intraperitoneally, chemically unrelated irritants are as effective as digitalis in causing emesis but intravenously the unrelated irritants do not cause emesis and digitalis does. Peripherally acting emetics act on intravenous injection as does digitalis, whereas several typical medullary stimulants and centrally acting emetics do not cause emesis in pigeons, thus indicating the peculiar rôle of digitalis as a systemic emetic without direct stimulation of the central mechanism.

Of the autonomic nerves the parasympathetics are indispensable to the emesis since vagotomy prevents it.

Swetlow, George I.: A Clinicophysiologic Study of the Pathway of Pain Impulses in Cardiac Disease. Am. J. M. Sc. 178: 345, 1929.

This paper is presented to correlate the previously observed clinical findings in patients complaining of severe cardiac pain with the information obtained by others through animal experimentation. The clinical observation showed that subjectively the patient was relegated to areas of the skin which were supplied by nerves arising between the eighth cervical and seventh thoracic spinal segments. These very same skin areas to which the patient subjectively referred to pain were hypersensitive to protopathic tests. These findings indicated that the pain impulses were passing through the rami communicantes and ganglia which were found between the eighth cervical and seventh thoracic spinal segments. The indifferent operative results ensuing from procedures upon the cervical sympathetic chain and

other nerves in the neck indicated by their failure to ameliorate the pain that the painful charges were not passing through these structures in their course to the sensorium. A review was made of 41 patients suffering from severe cardiac pain who were treated by paravertebral block. The gratifying results obtained seem to suggest that these rami communicantes and ganglia are the true conveying pathways of the pain impulses. The résumé of the animal experimentation supports the clinical observation.

Cowan, John, and Faulds, J. Steven: Syphilis of the Heart and Aorta. Brit. M. J. 285, Aug. 17, 1929.

The authors have studied a series of 390 cases presenting naked eye signs of cardiovascular disease and have found 60 of these cases to be syphilitic in nature. The various pathological lesions of syphilitic heart disease are discussed and correlated with the various clinical data. Under treatment the authors believe that the true treatment of cardiac syphilis is preventive, the successful treatment of primary illness and that cardiac syphilis is the result of an error on the part of the patient or his medical adviser.

Ernstene, A. Carlton: Observations on Coronary Thrombosis. Am. J. M. Sc. **178:** 383, 1929.

Three cases of coronary thrombosis with recovery and six cases terminating fatally have been studied. The recovered patients have been under observation for from one to about four years after the attack and all at present are enjoying satisfactory health.

Soon after the occurrence of coronary thrombosis there is commonly a marked reduction below normal of the vital capacity of the lungs. This observation is of diagnostic value because many patients at this time show few peripheral signs of myocardial failure. The conspicuously small cardiac contractions observed fluoroscopically after coronary occlusion are likewise of diagnostic assistance.

Progressive rise in blood pressure and vital capacity and increasing cardiac pulsations observed fluoroscopically are favorable prognostic signs. Conversely, falling blood pressure after the first few days, decreasing vital capacity and failure of the cardiac contractions to show improvement on fluoroscopic examination are unfavorable signs. Symptoms and signs indicative of extension of infarction are of very serious import.

The early recognition of coronary thrombosis is of importance because with proper management the patient may recover and live for years.

Chandlee, Gertrude Jackson, and Burvill-Holmes, E.: Clinical and Roentgen Ray Findings in the Study of the Heart and the Great Vessels. Am. J. M. Sc. **178:** 364, 1929.

The authors have studied 100 cases of heart disease of different types by physical examination, electrocardiographic records and roentgen ray examination. They believe that roentgen ray study helps to demonstrate the functional efficiency of the heart in respiration, the degree of pulsation and relative changes in the various areas of the heart and vessel walls and that the classification of hearts that are not normal as inspiratory or expiratory in type is explanatory and a functional classification of value. They discuss the effect of forced inspiration and expiration on the appearance of the heart in fluoroscopic examination.

The authors believe that the change in shape and position and measurements of the heart when these two observations are compared is of assistance and value in

establishing diagnoses of heart lesions and especially pointing out abnormal physiological function. They discuss the appearance of the heart silhouette when various pathological lesions are present.

Ackermann, W.: The Treatment of Tuberculous Pericarditis With Effusion by Injection of Air and Lipiodol Into the Pericardial Sac. Am. Rev. Tuber. 20: 236, 1929.

Report is made of a patient aged 48 with tuberculous pericarditis treated by repeated aspiration of the fluid of pericardial effusion. In all twenty aspirations were done, seventeen of which were followed by air injection into the pericardial sac and once by injection of lipiodol. Notwithstanding the various abnormal conditions of the pericardium the heart itself appeared normal in size throughout.

The author states that the performance of artificial pneumopericardium is without damage and discomfort, that the injection of air gives greater relief than does aspiration of the air alone, and that the presence of air delays the reformation of exudate. By holding apart the two layers of the pericardium the friction rub and the formation of adhesions are prevented. On x-ray examination, the air in the pericardium assists one to see how completely the exudate has been evacuated.

Cookson, Harold: A Case of Cardiac Syphilis With Ventricular Aneurysm. Brit. M. J. 94, July 20, 1929.

The author reports a case of aneurysm of the ventricle occurring in a woman aged 40 who had epigastric pain with signs of congestive heart failure preceding death by two years. A clinical diagnosis of aortic syphilis had been made.

Autopsy showed three aneurysmal sacs on the posterior wall of the (L) ventricle, the walls of which were of fibrous tissue containing considerable deposits of fibrin. All the valves, the aorta and the coronary vessels were normal. Microscopic section showed necrotic tissue banished by these fibrous tissues, the rest infiltrated by plasma cells and lymphocytes, the plasma cells predominating. The vessels surrounding the degenerative area showed marked obliterating changes and in some cases, the lumen was occluded. The condition had been present no doubt many years.

Giraldi, J. J.: The Histology of the Aortic Wall in Acute Rheumatism. Bristol M. Chir. J. 46: 145, 1929.

Five cases of rheumatic fever among four children and one man aged sixty have been studied. Lesions of a distinctive character have been found in the aortic wall in all of them. These lesions consist of areas of subacute inflammations around a small vessel of a nature similar to those found in the pericardium and other tissues in cases of rheumatic fever.

Yater, W. M.: Congenital Heart Block; Report of a Case With Incomplete Heterotoxy. Am. J. Dis. Child. 38: 112, 1929.

An infant was found to have a slow pulse at birth and an electrocardiogram showed complete auriculoventricular dissociation. The infant's pulse rate had been noted to be slower than the maternal rate before birth. There was cyanosis and other congenital malformations. Death occurred on the eighteenth day. Autopsy showed complete auriculoventricular dissociation. The infant's pulse rate had been position and relative to each other. Histological study showed a break in the continuity of the bundle of His and the author was unable to identify the right branch of the bundle of His. The electrocardiogram showed no sign of right bundle-branch block.

Book Reviews

Principles and Practice of Electrocardiography. By Carl J. Wiggers, M.D. St. Louis, 1929, 226 pages with 61 illustrations, The C. V. Mosby Co.

One method through which our knowledge of cardiac disease has been vastly increased during the past twenty years is by the use of instruments of précision, and of these latter none has given more definite information than the electrocardiograph. As a result there is a constant demand by physicians for postgraduate instruction in electrocardiography. The author of this volume, Professor Wiggers, has for years been giving courses in this field both at Cornell and at Western Reserve University. The use of the electrocardiograph, like the basal metabolism apparatus, has now become so extensive that personal instruction for all is no longer possible, and a book simply written is required for physicians and technicians who wish to instruct themselves in the theory and practice of electrocardiography. This book fulfills the need admirably.

The material of the book divides itself quite naturally into three parts, and of these the first part is the most difficult to present and the most valuable for the beginner. For here is explained in a clear and lucid manner the fundamental principles of electrocardiography and the physics of the galvanometer; finally there is an impartial review of all the important models of electrocardiographs available at present. Anyone working in this field is constantly asked to give his opinion on the relative merits of the various instruments on the market, and although the author quite properly does not make any specific recommendations, the reader obtains the necessary information about each model which should enable him to make his own selection according to his particular needs. This part on the instrument as such and directions for its use are especially helpful.

The second section describes the normal electrocardiogram and attempts to explain the meaning of the various curves. In this part the chapters on the significance of the electrical deflections are particularly well done, as it is most difficult to make this subject clear to medical students who have received no training in advanced physics or in electrophysiology. The author then proceeds to take up the usual abnormal records in logical sequence, and to correlate these abnormal electrocardiograms with the pathological physiology of cardiac disorders.

The third part places the reader in the position of a cardiologist who has to read the graphic records of clinical cases and interpret them.

This is analogous to the case system now so successfully used in medical and law schools. In each case there is first a description of the electrocardiographic findings, then an electrocardiographic diagnosis and the reasons therefore, then a brief description of the salient features of the disorder, with the relation to allied conditions (e.g., auricular flutter, impure flutter and fibrillation) and finally suggestions as to treatment.

The book is especially strong in the technic, in the instrumental aspect of the subject, and in the dynamics of the circulation—in those branches of the subject in which the author is an authority. The morphological aspects, e.g., the morbid anatomy as correlated to the electrocardiogram, are less emphasized, possibly because the author has had less personal experience in this field, possibly because he feels that we cannot speak with the same precision of the pathology of the heart as related to the electrocardiogram as we can of the physiology.

The frontispiece, a delicate and well-deserved tribute to the father of this science, contains an excellent portrait of Willem Einthoven.

As one reads this book, one cannot help remarking how much more definitely now than formerly many aspects of the whole subject can be presented to the beginner.

B. S. O.

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ACUTE ISOLATED MYOCARDITIS*

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THIS paper deals with the clinical and pathological observations on two cases of acute myocarditis, which is described in past writings as acute isolated diffuse myocarditis, acute isolated interstitial myocarditis, and Fiedler's myocarditis. These terms are used to designate a rare form of heart disease which presents both clinically and pathologically a picture different from that seen in other inflammatory lesions of the myocardium. The clinical picture in all recorded cases is clearly one of progressive myocardial failure, rapid in some cases, more gradual in others, but unassociated with any of the better known factors leading to heart failure. That such cases as have been reported were obscure, so far as etiology is concerned, is indicated by the fact that in no instance of the recorded cases which came to autopsy was a correct antemortem diagnosis made.

In the majority of instances the heart shows varying grades of hypertrophy and dilatation post-mortem. The myocardium alone is diseased, while the pericardium, endocardium and heart valves are not affected. Histologically, the inflammatory changes are confined largely to the interstitial tissues, although some authors find the parenchymatous tissue also involved. There is a diffuse infiltration of lymphocytes and polymorphonuclear leucocytes, especially eosinophiles, in the interstitial spaces. Aschoff[1] reports a case showing eosinophiles, plasma cells, lymphocytes, and a few fibroblasts, with slight necrosis of the muscle fibers. He mentions specifically that no rheumatic nodules were found.

The first clear account of this disease was given by Fiedler[2] in 1890, although two years earlier Steffen[3] reported two cases of acute myocarditis which probably fall in this classification. In a review of publications on the subject, we found reports of 36 cases with post-mortem study. The pertinent data of 30 cases in this group are contained in Table I.

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TABLE I

SUMMARY OF PREVIOUSLY RECORDED CASES OF ACUTE ISOLATED MYOCARDITIS CONFIRMED BY AUTOPSY*

NO.	AUTHOR	YEAR	AGE OF PATIENT	SEX	HEART	POSSIBLE ETIOLOGY	REMARKS
1	Steffen	1888	Between 45-50	–	Dilated		
2	Steffen	1888	50	–			
3	Freund	1893	40	♀	Dilated		
4	Rindfleisch	1898	34	♂	Hypertrophic		Blood culture showed staph. citreus.
5	Josserand and Gallavardin	1901	25	♂	Hypertrophic		
6	Josserand and Gallavardin	1901	29	♂	Hypertrophic		
7	Josserand and Gallavardin	1901	27	♂	Hypertrophic		
8	Zuppinger	1901	3	♂	Hypertrophic and dilated	Phlegmon left foot	
9	Zuppinger	1901	41	♂	Dilated	Burn	
10	Aschoff	1904	--	–			
11	Selletin	1904	16	♂	Hypertrophic	Carbuncle	
12	Selletin	1904	24	♀			
13	Förster	1905	6	–	Hypertrophic		
14	Saltykow	1905	37	♂	Hypertrophic	Abscess of neck	
15	Saltykow	1905	--	–	Enlarged		
16	Baumgartner	1916	20	♀	Hypertrophic		Possibly tbc. myocarditis.
17	Pal	1916	16	♀	Normal size	Gonorrheal urethritis	
18	Gierke	1921	25	♀	Hypertrophic		Possibly syphilitic myocarditis
19	Fiebach	1921	33	♀	Hypertrophic	Upper respiratory infection	
20	Fiebach	1921	63	♂	Enlarged		
21	Schilling	1921	22	♂	Hypertrophic		
22	Schilling	1921	63	♀	Hypertrophic		
23	Schmincke	1921	26	♀		Influenza	Early acute verr. endocard.
24	Hafner	1922	26	♀	Hypertrophic and dilated	Influenza	
25	Stolz	1922	21	♂	Hypertrophic	Rheumatism	
26	Lemke	1924	52	♂			
27	Lemke	1924	71	♀	Normal size	Pneumonia	Called acute parenchymatous myocarditis
28	Mordre	1924	41	♂			
29	Kaufmann	----	--	–		Infected burn	
30	Kaufmann	----	--	–		Infection of operative field	

*Fiedler's[2] origial four cases and one case each reported by Cohn[10] and Wolf[21] are not included in the above table because the original papers were not available to us.

The etiology of the disease is not determined. Aschoff[1] suggests that it probably has an infectious or toxic origin. Kaufmann[4] holds that it is due to the toxic action of bacterial products rather than to bacteria, since the latter have never been found in the myocardial lesions. Kauf-

mann refers to two cases that he has seen; one followed an infected burn which, however, healed, and the other followed an infection of the operative field due to the removal of tuberculous lymph nodes of the neck. Some writers associate the myocardial changes with certain infections which either antedated or which were present at the time of death. For example, Pal's[5] case was treated for acute gonorrheal urethritis two months prior to the onset of heart failure. Hafner's[6] patient developed myocardial insufficiency two months after an attack of influenza and died one month subsequently. In still other instances, there was no evidence of infection associated with the myocardial lesion,

Fig. 1.—X-ray (7-foot plate) of the heart in Case 1. Note the marked increase in the cardiac shadow to the right of the midline.

so that the attempts of past writers to establish the etiology of this form of acute myocarditis must be regarded as unconvincing.

Following are the observations we have made on two cases which appear to be examples of Fiedler's myocarditis.

CLINICAL REPORTS

CASE 1.—The patient, W. B., a white male, 36 years old, was admitted July 28, 1927, and died October 22, 1927. His chief complaint was shortness of breath and pain over the liver.

Past History.—He had the usual diseases of childhood and gave a vague history of a migratory arthritis at the age of 16, which, however, did not confine him to bed and for which he had no treatment. At the age of 26 he had an illness which forced him to stop work for nine months. This developed gradually, with dyspnea on exertion, and a few weeks later edema of the ankles appeared. After

nine months he recovered and returned to his work as a clerk in the courts. From this illness to the present one, ten years had elapsed, and during that time he had no illness and had been able to indulge in such activities as baseball and hockey with no undue breathlessness.

Present Illness.—Eighteen months before coming under our observation, the patient had an attack of influenza which confined him to bed only two days but which he regarded as marking the onset of his present difficulty. For the past year, he had more or less respiratory distress on exertion and lost considerable time from his work because of this symptom. He occasionally noticed slight edema of the ankles and tenderness over the liver. With rest in bed and digitalis for a few days, he recovered sufficiently to return to his work, only to fail again in a few weeks. The patient had been an invalid for two months before admission to the hospital.

Physical Examination.—This revealed a well-developed and well-nourished white male in no acute distress but with a rather marked systolic pulsation of the carotid arteries. There was no venous distension in the neck.

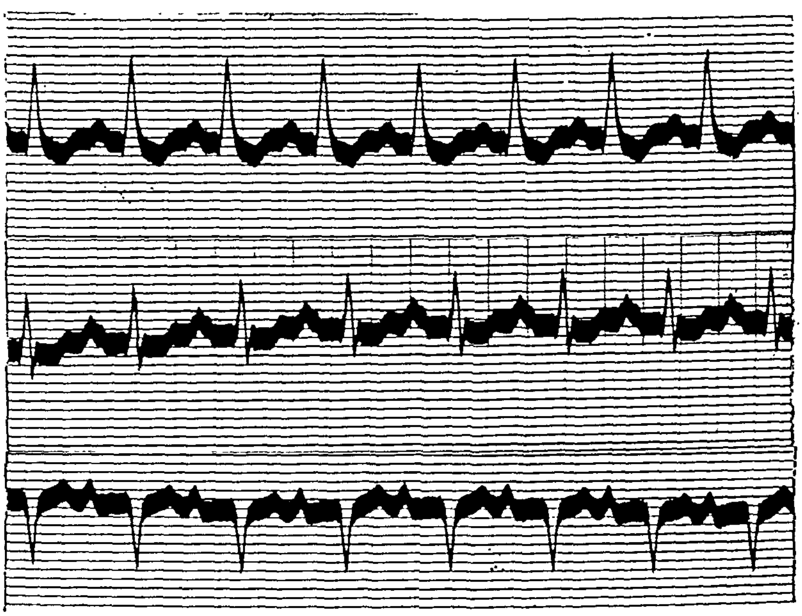

Fig. 2.—Three standard leads of the electrocardiogram in Case 1. In this and subsequent curves vertical lines represent time in 0.2 and 0.04 of a second; horizontal lines equal 10^{-4} volts.

Heart: There was a marked and extensive precordial activity visible over the upper part of the chest, most marked in the region of the right nipple. Palpation disclosed an unusual duplication of each cardiac impulse of about equal force. No definite apical impulse was distinguished. On percussion the limits of cardiac dullness extended to the left of the midline 9 cm. in the fourth and fifth intercostal spaces, and to the right of the midline 8 cm. in the third and fourth intercostal spaces. A seven-foot x-ray plate of the heart taken two days after admission is shown in Fig. 1. The cardiac shadow is greatly increased, particularly to the right of the midline. Auscultation over the apex revealed soft and muffled heart sounds, but no murmurs were heard. Approaching the base of the heart, the first sound was almost inaudible, but the second sound was loud, harsh and rasping. In the second intercostal space to the right, the sounds were again distant and almost inaudible. The heart sounds were loudest in the fourth right intercostal space, just inside the right nipple. Here one heard three heart tones equally spaced, the first two sounds corresponding to the double impulse described above.

A few moist râles were heard at the left lung base, otherwise the lungs showed nothing unusual. The liver edge was palpated 3 cm. below the costal margin; it was tender and pulsating. The pulses in all the accessible arteries were regular but very soft and easily compressible. The rate was 85 per minute and the systolic blood pressure was 100 mm. Hg. There was no thickening of the arterial walls demonstrable. The blood picture was normal, the blood Wassermann was negative, and the urine showed nothing unusual.

Clinical Course.—During the three months that this patient was under observation, he had a low grade fever with daily elevations to 38.2° C. Blood cultures were negative. The heart rate varied from 90 to 110 and the systolic blood pressure between 90 and 100 mm. Hg. No satisfactory determination of the diastolic blood pressure could be made. The cardiac findings showed little change. Two electrocardiograms were made; one on August 1, 1927 (Fig. 2), and the other October 19, 1927 (Fig. 3). These show moderate left ventricular preponderance. The changes in the S-T segment in Leads I and II are probably

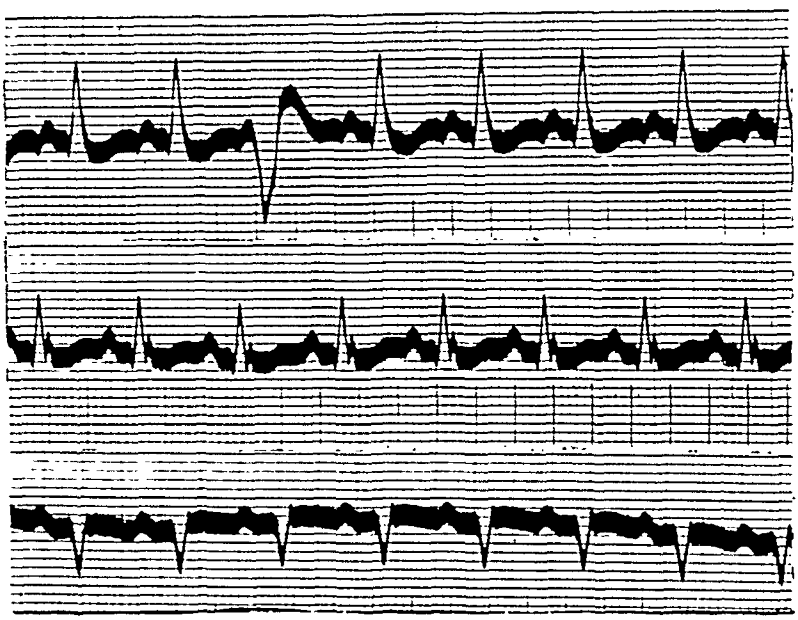

Fig. 3.—From the same patient, 79 days after Fig. 2.

due to digitalis. The patient gradually failed, the signs of congestion became more marked, and he died October 22, 1927.

The following clinical diagnosis was submitted: Rheumatic myocarditis; cardiac hypertrophy and marked dilatation; adherent pericardium (?); death due to myocardial insufficiency.

Pathological Report.—The autopsy was performed four hours after death. The body was that of a well-developed and well-nourished, adult white male, 36 years old. There was marked edema of both lower extremities and the subcutaneous tissues were very moist. The left pleural cavity contained 600 c.c. of a straw colored, clear liquid, but the pleural surfaces were smooth and glistening, and there were no adhesions. The other body cavities appeared normal. Multiple red infarcts were found in the lower lobe of the left lung, and old and recent infarcts were present in both kidneys. Both the liver and kidneys showed extensive cloudy swelling. Except for marked chronic passive hyperemia the other abdominal viscera showed no gross pathological changes.

Heart: The heart weighed 600 grams. The organ was globular in shape and

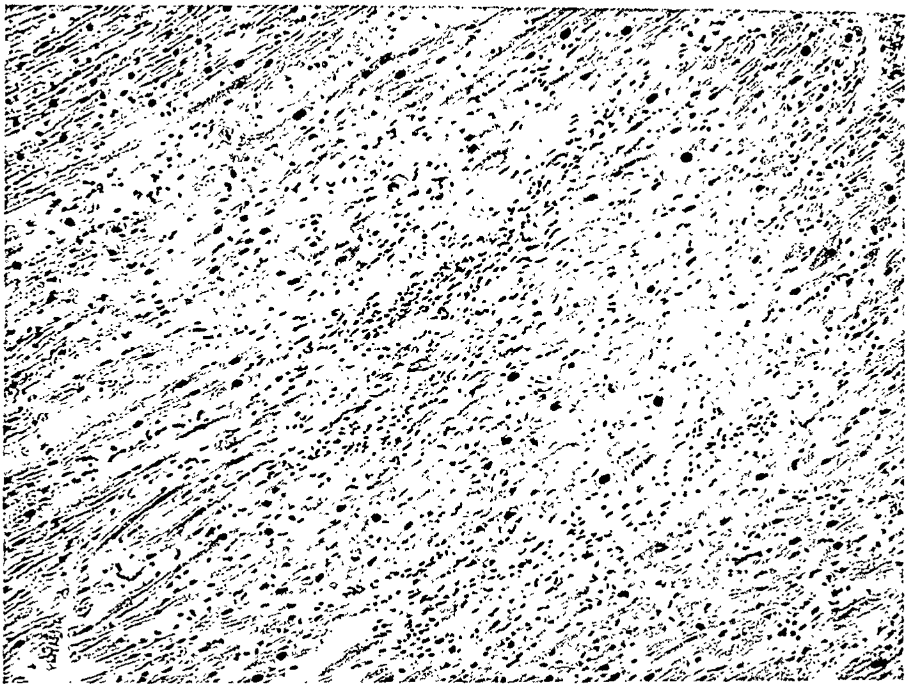

Fig. 4.—Section of myocardium, Case 1. Hemosiderin-eosin stain x 60. Description in text.

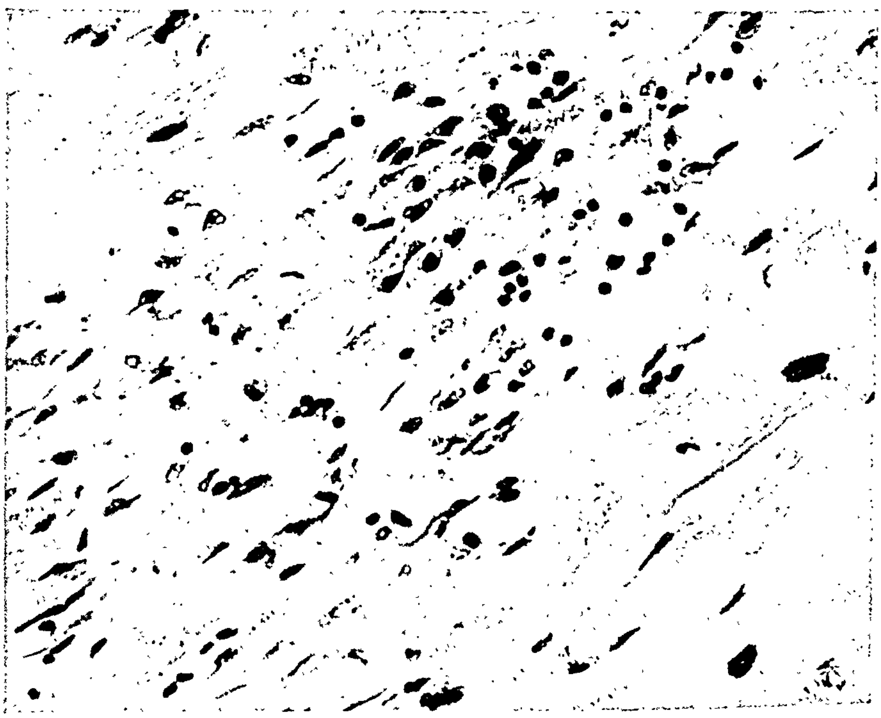

Fig. 5.—Section of myocardium, Case 1. Hemosiderin-eosin stain x 300.

markedly enlarged in all chambers. The apex was very flabby, rounded, and formed in part by the right and in part by the left ventricle. The epicardium was smooth and glistening throughout, and the coronary vessels were not diseased. The mural endocardium of the right ventricle showed several thrombi, grayish-red in color, which were firmly attached to the wall. The valves throughout were tender and delicate and showed no retraction or fibrosis. The aortic valve showed only two leaflets. The mitral valve had a circumference of 16 cm., the aortic 8 cm., the pulmonary 10.5 cm., and the tricuspid 16 cm. The sinuses of Valsalva were smooth. The papillary muscles and columnae carneae were hypertrophic and flattened. On cut section the myocardium was reddish-gray in color; it showed a coarser architecture than normal and contained many grayish-yellow streaks.

Microscopical Description.—The heart muscle fibers were larger than normal, the striations were obscure, and the nuclei showed squared ends and appeared swollen. Throughout the interstitial tissue there was an extensive infiltration of endothelial cells, plasma cells, and lymphocytes (see Figs. 4 and 5). The endothelial cells in some fields had a dark, slightly granular cytoplasm with sharply defined nuclei, but no Aschoff bodies or necrotic areas were seen. A few areas showed in addition polymorphonuclear leucocytes and many eosinophiles. Fibroblasts were seen in some fields; in others, small blood vessels around which were many lymphocytes, endothelial cells and polymorphonuclear leucocytes. Only a few sections showed these inflammatory cells invading the heart muscle fibers. There was a slight increase in connective tissue, but no fibrin or giant cells were noted. In a few sections were seen segmentation of the heart muscle fibers. Sections stained with Gram-Weigert stain showed no bacteria. Similarly the Warthin-Starry and Levaditi method gave a negative result for spirocheta pallida.

Pathological Diagnosis.—Acute myocarditis; hypertrophy and dilatation of the heart; relative insufficiency of mitral, tricuspid and pulmonary valves; mural thrombi of the right ventricle; multiple infarcts of left lung and both kidneys.

CASE 2.—The patient, S. W., a colored male laborer, 48 years old, was admitted to the Psychopathic Division of the Cleveland City Hospital, September 16, 1927, because of mental symptoms, but it was apparent on examination that he was suffering from heart disease. Exact information concerning the duration and progress of the present illness was not obtained. However, it was learned that the patient worked as a laborer until seven months before admission when he stopped because of breathlessness on exertion. During this period he was not incapacitated, he had no objective signs of circulatory failure and continued to go about until a few days before coming under our observation.

Past History.—There was a vague history of a penile lesion fifteen years ago. The patient had always worked as a day laborer and had never been confined to bed. He was the father of ten living children, and the wife's history showed no miscarriages. He was a moderate drinker but consumed no narcotic drugs.

Physical Examination.—The physical examination revealed the typical clinical picture of a patient suffering from moderate circulatory failure. In the semi-upright position the veins of the neck were engorged, and he was obviously dyspneic. The lungs were clear except for râles of congestion at both lung bases. There was no visible apical thrust, but palpation revealed a rather diffuse, feeble apex beat in the sixth intercostal space, 2 cm. to the left of the midclavicular line. The first heart sound was entirely replaced by a systolic murmur, and over the conus and base of the heart the sounds were muffled but no murmurs were heard. The cardiac mechanism was normal but was interrupted occasionally by an extrasystole. The pulse in the accessible arteries was markedly diminished in volume, and the blood pressure was 130/100 mm. There was moderate sclerosis of the arterial walls. The liver was 2 cm. below the costal margin and tender. Other-

wise examination of the abdomen was negative. There was moderate edema over the sacrum and over the shins. The patient had no fever, a normal blood picture, and except for albumin the urine showed nothing unusual. Tests for syphilis in both blood and spinal fluid were entirely negative.

Fluoroscopically the heart showed a marked increase in the transverse diameter, particularly to the right. This is shown in the seven-foot x-ray plate reproduced in Fig. 6.

Clinical Course.—The patient showed no signs of improvement during the forty-eight days that he was under observation. A week before death his temperature rose abruptly to 39.5° C., and then continued as a septic type of fever until he expired. The congestive failure increased, the heart sounds became feebler, the blood pressure gradually dropped to as low as 85 mm. systolic, and in this con-

Fig. 6.—X-ray photograph (7-foot plate) of the heart in Case 2. Note the increase in the cardiac shadow both to the right and left.

dition he died. Five days before death an electrocardiogram (Fig. 7) was taken which shows left ventricle preponderance but otherwise nothing remarkable.

From the clinical observations on this patient it was apparent that death resulted from circulatory failure, but in the absence of hypertension, and with no clear evidence of valve disease, the etiology of the heart failure was obscure. After much discussion, the following clinical diagnosis was submitted: Coronary arteriosclerosis; myocardial fibrosis; cardiac hypertrophy and marked dilatation; death due to circulatory failure.

Pathological Report.—The body was that of a well-developed and well-nourished adult colored male with marked edema of both lower extremities. Both pleural cavities contained a small amount of fluid, but the pericardial and peritoneal cavities appeared normal. Infarcts were found in the left lung, in both kidneys and in the spleen. Both the liver and the kidneys showed marked cloudy swelling. Chronic passive hyperemia was found in all the viscera.

Heart: The organ was soft and friable, dilated in all chambers and weighed

700 grams. The coronary vessels were not tortuous and showed only minimal intimal changes with no calcification or thrombosis. Several firmly attached thrombi were found in the endocardium of the left ventricle, where a few circumscribed areas of endocardial fibrosis were seen. The heart valves were carefully inspected, but no old or recent changes were found. The aortic valve was 8.5 cm. in circumference, the mitral 13 cm., the pulmonary 9 cm., and the tricuspid 14 cm. The papillary muscles were large and flattened. The architecture of the myocardium on cut section was obscured, and throughout there were many small, soft, red and yellow areas, but no infarction was found. The right ventricular wall measured 3 mm. in thickness and the left 15 mm.

Microscopical Description.—There is a marked infiltration of lymphocytes, endothelial cells and polymorphonuclear leucocytes in the interstitial spaces (see Figs. 8 and 9). However, a few sections show these changes also in the parenchymatous

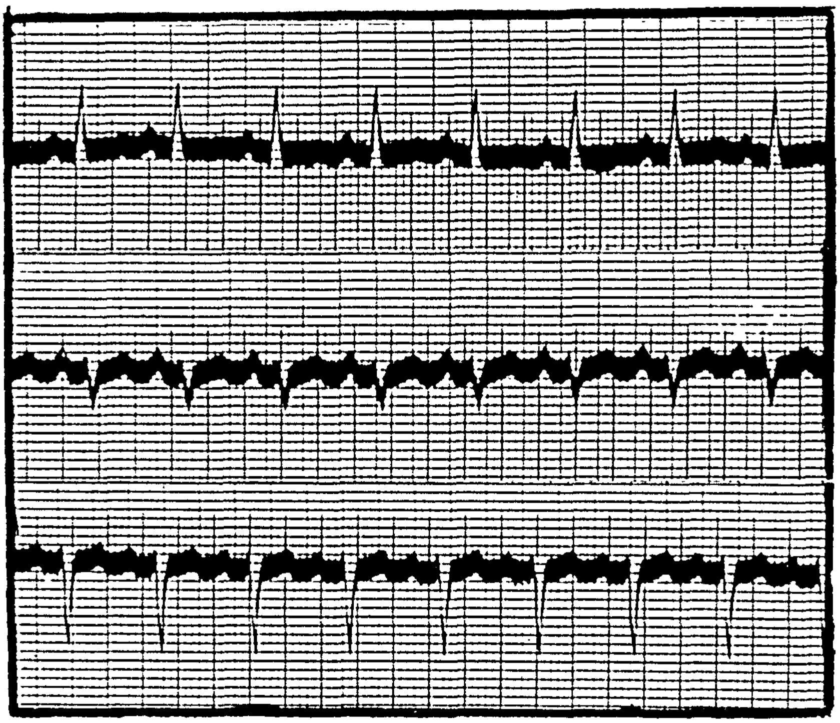

Fig. 7.—Three standard leads of the electrocardiogram in Case 2 showing a normal mechanism with moderate preponderance of the left side.

tissue. In some sections, endothelial cells and lymphocytes predominate, while in others one sees many eosinophiles and a few plasma cells. Large endothelial cells with eccentrically situated nuclei, together with a few myelocytes and polymorphonuclear leucocytes are found. Some fields show massive infiltrations of these cells. In some sections there is a new formation of small blood vessels which show extravasations of red blood cells, together with lymphocytes and endothelial cells. No increase in connective tissue is observed. The heart muscle fibers appear swollen, the cytoplasm granular, and there is a definite loss of striation. In some fields showing marked inflammatory changes, the muscle fibers are shattered. No giant cells or Aschoff nodules are seen. A careful search for bacteria and for spirocheta pallida gave a negative result.

Pathological Diagnosis.—Acute and subacute myocarditis; hypertrophy and dilatation of heart; mural thrombi of the left ventricle; multiple infarction of lungs, spleen and kidneys.

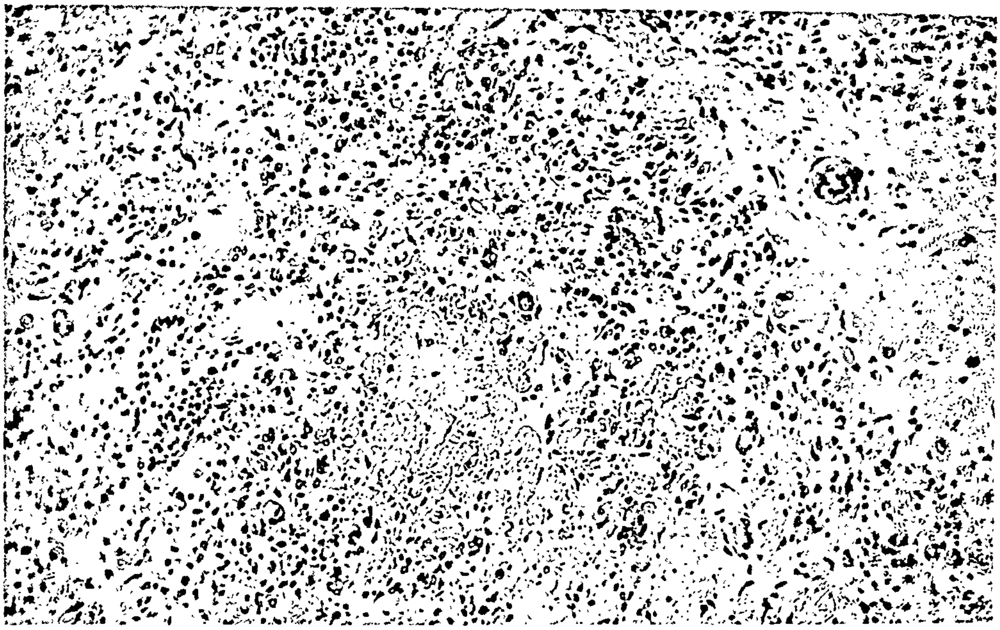

Fig. 8.—Cross-section of the myocardium in Case 2. Hemosiderin-eosin stain x 120. Description in text.

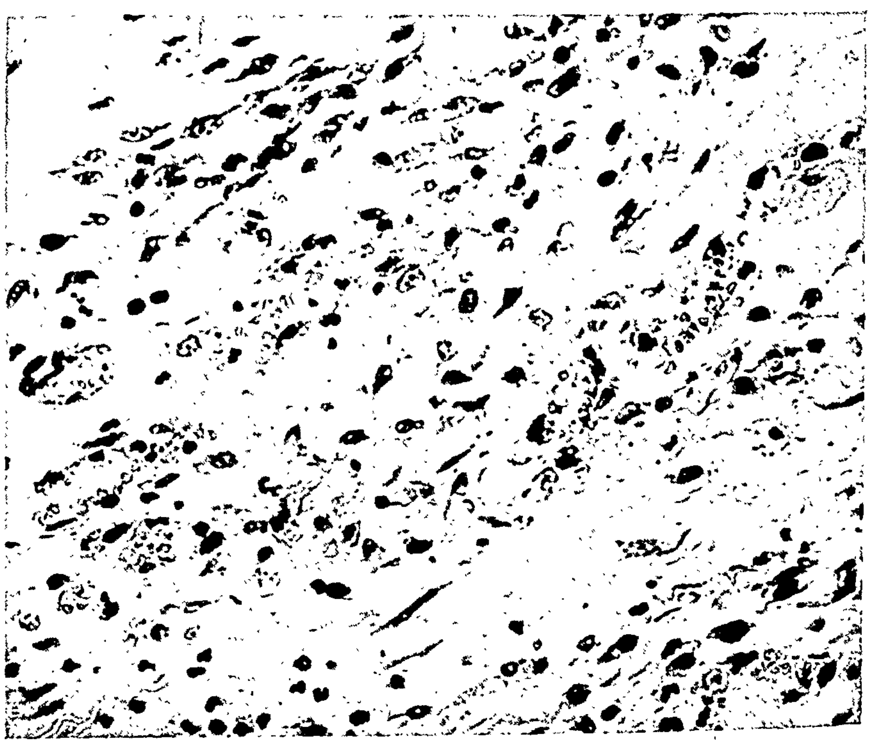

Fig. 9.—Section of the myocardium in Case 2. Hemosiderin-eosin stain x 300. Note the large endothelial cells.

DISCUSSION

It was apparent that progressive myocardial insufficiency dominated the clinical picture in the above two cases, but the etiological factors underlying the heart failure were obscure. Both cases showed clear evidence of marked cardiac enlargement, but no signs of valve disease or hypertension. In Case 2 there was no history of rheumatic infection, no evidence of syphilis, and no history of an acute infection antedating the appearance of heart failure. So far as one could tell, the patient's symptoms appeared insidiously, and in spite of treatment he went rapidly downhill to death from circulatory failure. One observes patients, usually males beyond forty, who present just such a clinical picture and who show at post-mortem extensive fibrosis of the ventricular muscle secondary to coronary arteriosclerosis. This process appeared as the most likely etiological factor in Case 2.

In Case 1, the final clinical diagnosis was even more difficult to establish. The nature of the cardiac affection ten years previously, with edema, breathlessness, and precordial pain, was obscure. This had disabled the patient for several months, but he apparently made a complete recovery. To complicate the picture further was the vague history of rheumatism at the age of 16 years. Although the clinical findings were by no means characteristic of rheumatic heart disease, yet in the light of the previous history rheumatic involvement of the myocardium seemed the most likely etiological factor, hence this clinical diagnosis was submitted.

At autopsy the hearts in the two cases were similar; they were flabby, dilated and hypertrophic, and on cut section presented clear evidence of a damaged myocardium. However, the endocardium, the valve apparatus, and the pericardium appeared normal. Histologically both hearts showed extensive inflammatory changes, chiefly in the interstitial tissue but also involving the parenchyma. The widespread muscle damage afforded an adequate explanation for the progressive circulatory failure observed during life, but a microscopic study of the myocardial lesions threw no light on the etiology of the disease. This statement of opinion is made in full appreciation of the difficulties in eliminating rheumatic infection as the etiological factor in our cases. For this reason a careful search for Aschoff nodules was made, but none were found.

It is of course conceivable, as Sacks[7] states, that diffuse infiltrations of the myocardium may represent exaggerated examples of the less conspicuous leucocytic collections which regularly accompany the Aschoff body. If this be true, then our cases as well as those previously recorded may be examples of rheumatic involvement of the myocardium, but this question—difficult either to prove or to disprove—is by no means settled, and until evidence to the contrary is established, we believe that the cases here reported belong in the group of so-called acute isolated myocarditis. To regard such cases as rheumatic would, in the light of our present knowledge, contribute nothing to the solution of the problem.

The cause of the cardiac hypertrophy in this disease is a tempting speculation. For example, the heart in Case 1 weighed 600 grams; in Case 2, 700 grams, and in the majority of the previously reported cases the heart was heavier than normal. Some authors believe that myocardial fibrosis leads to hypertrophy, and this assumption is used to explain the increased size of muscle fibers in the vicinity of infarcts. That the minimal fibrotic changes seen in our cases led to the hypertrophy found, seems a far-fetched assumption. A more reasonable explanation is that recently suggested by the work of Eyster.[8] He found in dogs that dilatation of the heart was the initial and immediate reaction to an experimental lesion. After a period of a few days, the heart returns to its normal size and hypertrophy then gradually develops, reaching a maximum for a single lesion in about eighty days. Eyster also made this significant observation; that hypertrophy ensues in spite of the fact that the experimental lesion (aortic stenosis produced by rubber-band ligatures about the root of the aorta) is removed after a few days and during the period of dilatation. It appears from Eyster's experiments that the stretching of the heart muscle from dilatation supplies the stimulus for the subsequent development of hypertrophy. On the basis of these experimental observations it is conceivable that widespread inflammatory changes in the myocardium, as found in our two cases, may lead to dilatation of the heart, and this in turn to hypertrophy.

Eyster, however, dealt with a myocardium which was not the seat of disease. The dilatation in his cases was what is referred to as passive dilatation, in which the chamber is dilated because of an absolute increase in intracardial pressure. The dilatation incident to myocardial disease is referred to as active dilatation. Here the muscle, because of inherent weakness incident to disease, permits of dilatation without the interposition of factors which raise intracardial pressure. Various observations indicate that stretching of the muscle in diastole induces hypertrophy but that this fact applies to those cases in which the muscle is the seat of concurrent degenerative disease is open to doubt. There is at least a reasonable question as to whether or not such diseased muscle is capable of the increased nutritional function which would appear to be necessary for hypertrophy to occur.

The assumption that hypertension existed at some period in the lives of these two patients might explain the hypertrophy, but would not explain the myocarditis. Furthermore, the coincidence of hypertrophy, myocarditis and dilatation in all the cases reviewed would require similar assumption of hypertension in such young individuals that it would be practically untenable.

It is unfortunate that there is no uniform terminology for the type of myocarditis here reported. Past writers use the term "interstitial," "circumscribed," "diffuse," "isolated," and "idiopathic," singly or

in combination to describe the disease. Since primary involvement of the myocardium is the most characteristic clinical and pathological feature of this disease, it seems to us that the term "isolated myocarditis," acute or subacute, is the most appropriate.

SUMMARY

The clinical and pathological observations on two cases of acute isolated myocarditis of undetermined etiology are recorded, together with a tabulation of the pertinent data in thirty similar cases previously reported.

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STUDY OF THE R-T INTERVAL IN MYOCARDIAL INFARCTION*

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CORONARY occlusion with myocardial infarction has come to be considered a distinct clinical entity, the diagnosis of which can be made during life with a high degree of certainty. The first combined clinical and electrocardiographic observations following acute coronary occlusion were reported by Herrick. The electrocardiogram, taken forty-three days after the occlusion, and published by him (Fig. 1), showed relatively late changes in the R-T interval following infarction of the myocardium in the region supplied by the anterior descending

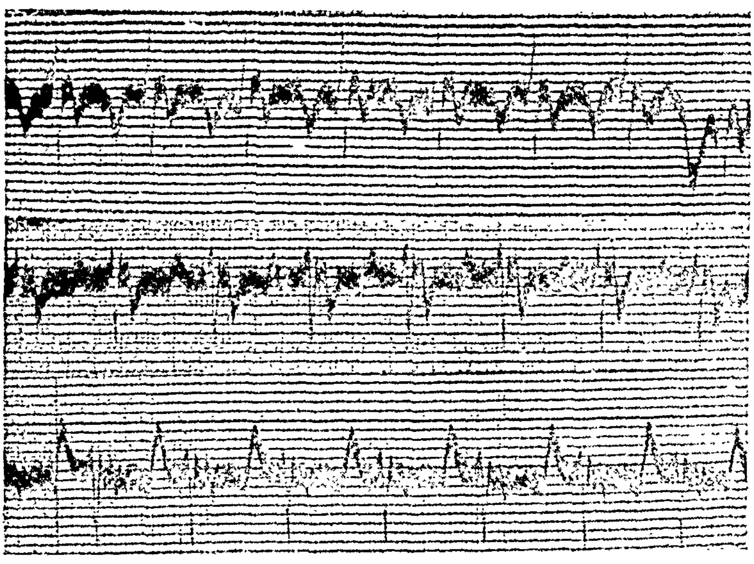

Fig. 1.—Electrocardiogram taken May 3, 1917, forty-one days after the symptoms of coronary obstruction. Digitalis not used at this time. (From Herrick.)

branch of the left coronary artery. This tracing is a classical example of the T_1 type of changes which will be described later in this paper. At the end of his article Herrick made this rather prophetic statement: "The thought has been that if it can be proved that with a certain artery obstructed there is a definite lesion in the heart-muscle or in the conducting system, and if with that lesion there is a definite electrocardiogram, may we not, when we encounter that abnormal electrocardiogram in the human being, particularly if he has had symptoms suggestive of coronary thrombosis, be able to state with a reasonable degree

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of certainty that the patient has had obstruction in a particular portion of the coronary system? May it perhaps be possible to localize a lesion in the coronary system with an accuracy comparable to that with which we locate obstructive lesions in the cerebral arteries?''

Smith reported alterations of the T-waves and of the R-T segment occurring more or less constantly after ligation of the branches of the left coronary artery in dogs and mentioned that similar changes in man were to be observed in the case reported by Herrick. Pardee[9] observed

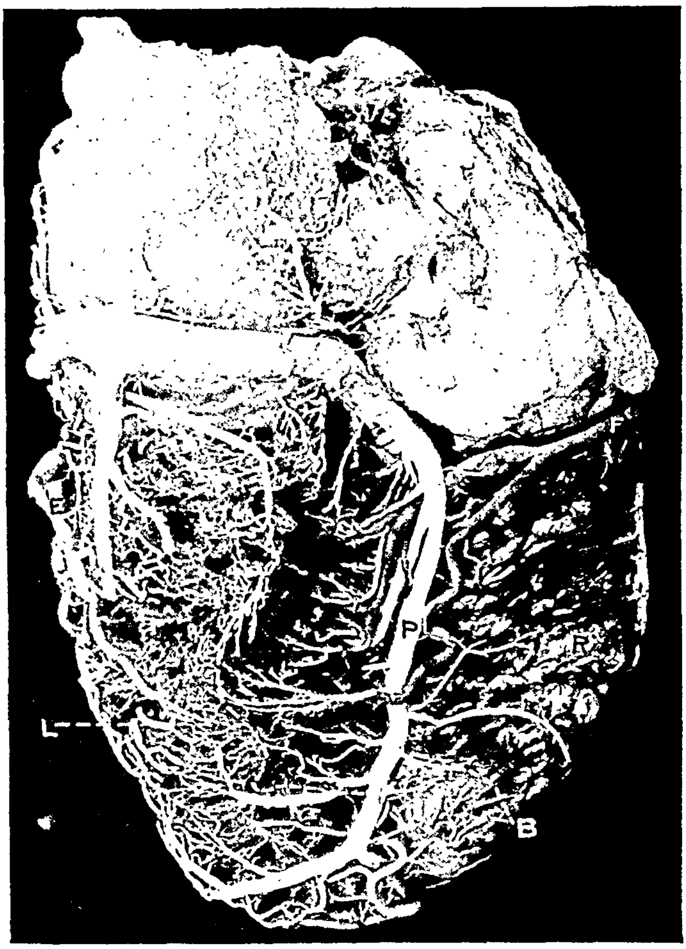


Fig. 2.—Posterior view, after preparation by celluloid-corrosion method, of heart from a man forty-two years old. *R*, right ventricle; *L*, left ventricle; *E*, left coronary artery; *F*, right coronary artery; *P*, posterior interventricular vein; *A—B*, line separating the portions of the heart supplied by the right and left coronary arteries. This represents almost the average normal line of separation except in the base of the left ventricle where the circumflex branch of the left coronary artery supplies a little more of the posterior surface than is usual.

and described in man a type of deformity of the R-T segment such as Smith had obtained in dogs following ligation of branches of the left coronary artery and designated this the coronary T-wave.

Many observers have contributed electrocardiographic tracings in man corroborating the observations of Smith and Pardee.[9] In a recent excellent contribution Parkinson and Bedford reported the electrocardiographic changes occurring in twenty-eight cases following infarc-

tion. They have extended our knowledge of the variations in the changes of the R-T segment associated with infarction and have suggested the classification of these variations into two main types.

A thorough knowledge of the distribution of the coronary arteries is of paramount significance in any attempt to interpret the electrocardiographic changes occurring in myocardial infarction. Therefore it seems advisable to emphasize certain observations on the blood supply of the heart before proceeding further in this study. The anatomical data which we present were obtained from a study of hearts of human beings injected by the celluloid and corrosion method, which Whitten has described.

Spalteholz, Gross and others have emphasized that there is considerable variation in the coronary circulation in normal hearts. The supply of the posterior surface of the left ventricle probably is most variable, and a detailed knowledge of the variations in the blood supply of this region is of the greatest importance for reasons which will become obvious.

The right coronary artery enters the coronary sulcus shortly after it takes origin from the aorta. Continuing in this groove, which lies at the juncture of the right auricle and the right ventricle, it passes to the posterior surface of the heart. As it goes around the right side of the heart, branches are given off at intervals, and these generally course in the direction of the apex. At the point where the right coronary artery crosses the posterior interventricular sulcus, it gives off a large branch, the posterior descending artery (Fig. 2). The latter vessel generally extends down the posterior interventricular sulcus from two-thirds to three-fourths of the distance from the coronary sulcus to the apex. *This artery supplies approximately the posterior third of the interventricular septum.* At the point of origin of the posterior descending artery, the right coronary artery generally crosses the posterior interventricular sulcus to reach the posterior surface of the left ventricle. Here the right coronary artery usually divides into two or three branches, which, turning rather sharply, course about three-fifths of the distance from the coronary sulcus to the apex. These vessels usually do not extend to the left beyond a line midway between the posterior interventricular sulcus and the obtuse or left margin of the heart.

There are two definite variations from the average normal right coronary artery. Sometimes the posterior descending artery and the branches of the right coronary artery which reach the posterior surface of the left ventricle extend to the apex and occasionally slightly beyond this point (Fig. 3). In this case, the right coronary artery supplies practically the whole posterior surface of the left ventricle, a portion or all of the apex, as well as the posterior third of the interventricular septum.

At times, the right coronary artery is relatively unimportant and

does not reach the posterior interventricular sulcus or the posterior surface of the left ventricle. In that event it is evident that the left coronary artery must supply the entire posterior portion of the left ventricle as well as the whole interventricular septum (Fig. 4). This is accomplished by the circumflex branch of the left coronary artery, which becomes of unusual importance, and proceeds along the base of the left ventricle, at the level of the atrioventricular juncture, finally to reach the posterior interventricular sulcus down which it courses

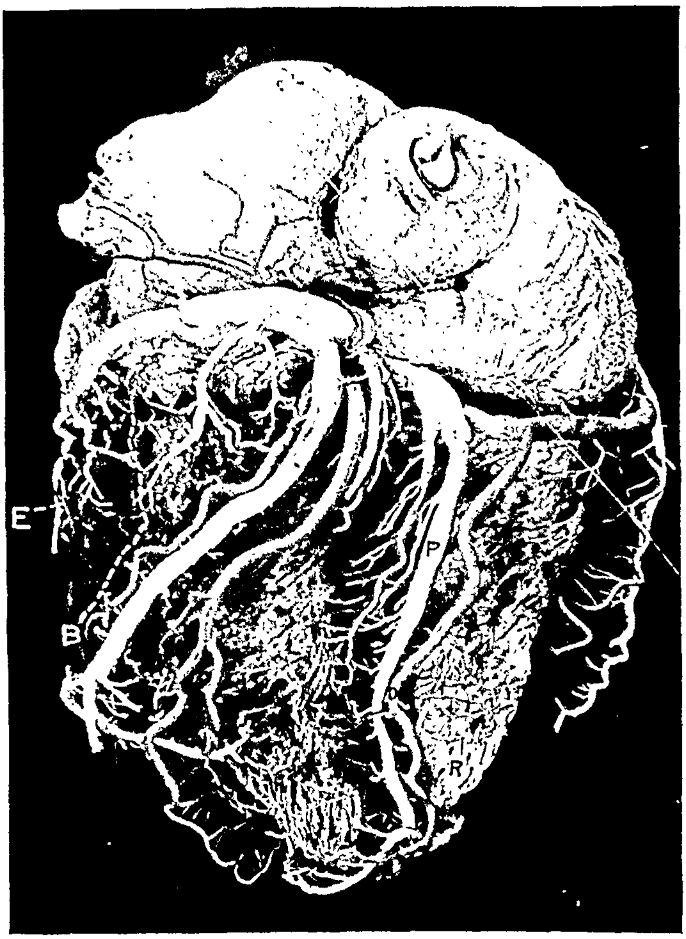


Fig. 3.—Posterior view of heart after preparation by celluloid-corrosion method. The right coronary artery supplies the entire posterior surface of the left ventricle and the apex. *R*, right ventricle; *L*, left ventricle; *P*, posterior interventricular vein; *D*, posterior descending artery (right coronary); *A—B*, line of separation of parts of left ventricle supplied by right and left coronary arteries; *E*, left coronary artery; *F*, right coronary artery.

toward the apex to become the posterior descending (or interventricular) artery.

The left coronary artery is generally considered to have two main branches. The largest, the anterior descending artery, proceeds down the anterior interventricular sulcus to the apex, and from this point it generally extends on to the posterior surface of the heart, coursing up the posterior interventricular sulcus usually from a fourth to a third of

the distance toward the base of the ventricles. As the artery passes down the anterior surface of the heart, it gives off large branches to supply the anterior surface of the left ventricle and the anterior two-thirds of the interventricular septum, but it gives only a few small vessels to supply the anterior surface of the right ventricle.

The other main division of the left coronary artery is known as its circumflex branch. It arises near the origin of the left coronary artery and courses immediately to the left, following the *coronary sulcus for a* variable distance. It generally passes around the obtuse or left margin

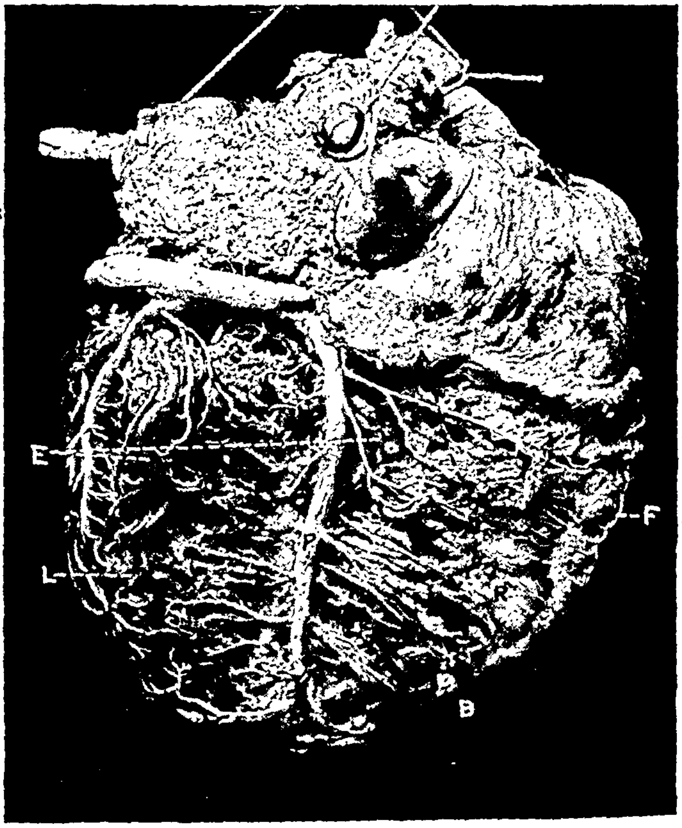


Fig. 4.—Posterior view, after preparation by celluloid-corrosion method, of heart from a woman fifty-five years old. The left coronary artery supplies the entire posterior surface of the left ventricle and a portion of the posterior surface of the right ventricle. *R*, right ventricle; *L*, left ventricle; *P*, posterior interventricular vein. *A—B*, line of separation of portions of right ventricle supplied by right and left coronary arteries; *E*, left coronary artery; *F*, right coronary artery.

of the heart to reach and supply the left third or half of the posterior surface of the basal three-fifths of the left ventricle. That this artery occasionally assumes additional significance and extends to the posterior interventricular sulcus has been mentioned in the discussion of the variations of the right coronary artery.

In the average normal heart the left coronary artery supplies the entire anterior surface of the left ventricle, the adjacent third of the anterior surface of the right ventricle, the apex of both ventricles, all of the interventricular septum at the apex, the anterior two-thirds of

the septum above that point, and the left half of the posterior surface of the left ventricle. The right coronary artery usually supplies two-thirds of the anterior surface and all of the posterior surface of the right ventricle with the exception of the apex. It also generally supplies the posterior third of the interventricular septum (except at the apex), and the adjacent half of the basal three-fifths of the posterior surface of the left ventricle.

In a separate article one of us (Whitten[16]) has shown a vast difference between the branches of the right coronary artery supplying the right ventricle, and the branches of the right and left coronary arteries supplying the left ventricle. These arteries supplying the right ventricle appear to spread out over the heart in the same general plane as the subdivisions of the artery from which they arise. The wall of the left ventricle is much thicker than that of the right. The branches which supply the former, whether they originate from the right or the left coronary artery, course along the surface of the heart just beneath the epicardium. Their branches do not spread out in the same general plane. Instead, they leave at right angles and penetrate straight through the myocardium, giving off very few branches until they reach the endocardium where they again turn at a sharp angle and end in a mass of fine arterioles.

The left coronary artery is immobilized to a considerable degree by these branches which penetrate the myocardium at right angles. The smaller branches of the right coronary artery, which supply the right ventricle, do not possess any conspicuous deep branches. On the contrary, the main branches which supply the posterior interventricular septum and posterior portion of the left ventricle are immobilized in a manner similar to that in which the branches of the left coronary artery are immobilized. In its first portion, the right coronary artery has much greater mobility than the left. It seems reasonable to believe that the architecture of the branches of the left and right coronary arteries is significant in the occurrence of occlusion in these vessels and, furthermore, suggests a reason why occlusion of the right coronary artery is manifested chiefly by infarction in the posterior portion of the left ventricle.

The anterior descending branch of the left coronary artery courses straight except for the tortuosities that occur with increasing age. As this vessel is anchored securely by deep vessels passing into the septum, the tortuosities often become marked. The right coronary artery, while crossing the right side of the heart, swings in an arc making a complete semicircle. If this vessel becomes sclerosed, it does not become very tortuous because it is free to project farther from the surface of the heart and simply swings around in a larger arc. It is suggested that this is a protection to this part of the right coronary artery.

It is possible that other anatomical factors, such as anastomosis or

the thebesian circulation, also may render the right ventricle more or less immune to infarction.

Myocardial infarction may be acute or chronic, or acute infarction may be superimposed on chronic infarction. Acute infarction results from sudden, complete occlusion of a coronary artery or one of its branches. Following this over a long period, fibrous tissue gradually replaces the infarcted muscle fibers to an extent which will depend largely on the effectiveness of anastomotic circulation in that region. This end stage of acute infarction is often difficult to distinguish from the chronic type which results from the gradual, almost complete obliteration of the lumen of a coronary vessel that goes to a particular region, although in chronic infarction the fibrosis is more likely to assume a more patchy distribution. It seems probable that gradually developing chronic infarction may not be signalized by dramatic events, with severe pain, such as are seen in acute infarction. It is even probable that it may occur with little if any pain, judging from our clinical records. We agree with Pardee that it is probable that chronic infarction, provided it produces focal rather than diffuse change, is capable of bringing about the typical alteration of the R-T segment seen in acute myocardial infarction.

The criteria for the recognition of changes in the electrocardiogram indicative of myocardial infarction have been established fairly well. Pardee, in 1920, called attention to these changes in clinical electrocardiograms and in 1925 amplified these observations. He stated that the characteristics of the electrocardiogram in myocardial infarction were the presence in one or more leads, usually only in one, of a downward, sharply peaked T-wave with an upward convexity of the S-T or R-T interval. When this change in the T-wave occurred in the third lead only, he considered that the change was not significant, unless the T-wave was inverted in Lead II, although convexity of the segment preceding the T-wave in Lead II need not be present. In his original description he pointed out that the T-wave does not start from the zero level, that it quickly turns away from its starting point in a sharp curve and ends in a sharply peaked T-wave somewhat larger than normal.

Parkinson and Bedford have contributed much to the criteria of recognition of the changes in the R-T interval in infarction.* They found, as did Pardee, that the R-T segment arose below or above the isoelectric line, best seen in Leads I and III and occurred "constantly in opposite directions in these two leads; thus an R-T elevation in Lead I is associated with an S-T depression in Lead III and vice versa." However, they found that an R-T deviation may be found in a single lead or in combined Leads I and II, or II and III in which case the deviation

*Hereafter in this paper the designation R-T will be used to include the segment between the QRS complex and the end of the T-wave. At times this will actually be the S-T segment.

was in the same direction in the two leads. They recognized various contours of the R-T interval; it may be a flat-topped plateau, descending gradually to the iso-electric level; it may rise gradually, reaching a summit at the end of the plateau, or it may form a dome-shaped elevation at the end of which the peak of a negative T-wave may occur. These authors emphasized that when R-T deviation was marked, T-waves, strictly speaking, were not evident. They pointed out that in these cases the T-waves approximated the monophasic type. The R-T deviation was transient and usually when repeated electrograms were made, was disappearing before the negativity of the T-wave was well developed.

Parkinson and Bedford further divided the curves into types T_1 and T_3, types depending on whether the T-waves were inverted in Lead I or in Lead III. Differing from Pardee, they concluded that a sharply pointed, inverted T-wave in Lead III "may be the only relic of a previous cardiac infarction." Although we have no case in which we can obtain positive evidence on this point, we believe that it is probably a justifiable conclusion.

In interpreting electrocardiograms of infarction it is of the utmost importance to know the time they were taken in relation to the time when the infarction probably occurred. In the first week after infarction change of level and contour of the R-T segment is likely to occur, and frank inversion of the T-wave often is seen only after this. Multiple electrocardiograms often enable one to identify changes in the R-T segment that are indicative of infarction and that are not clearly shown in a single tracing. A careful inspection of the changes in the R-T interval in Lead II, particularly with the purpose of determining to which of the two other leads it bears the closest resemblance, will furnish the safest guide to the classification into types T_1 and T_3. Thus, the elevation and rounding of contour of the R-T segment in Leads I and II will serve to identify the abnormality as of type T_1, although no inversion of the T-waves is present; the same phenomena in Leads II and III will place the tracing in the group T_3. Occasionally in Lead I the identification of an abnormality of type T_1 depends on an inverted T-wave in that lead, with R-T characteristics preceding it which suggest infarction. We have not encountered any instance in which we could unquestionably place a tracing in the type T_3 on the basis of R-T changes in Lead III unattended by somewhat similar changes occurring in Lead II. All degrees of bundle-branch block must be carefully excluded before an electrocardiographic tracing may be said to be characteristic of myocardial infarction. Care must be exercised in interpreting changes in the R-T interval in electrocardiograms which give evidence of auricular fibrillation. Furthermore, certain cases of hypertension will cause changes in the level of the R-T

interval which closely simulate the late changes in the electrocardiogram following infarction.

In recapitulation, the early changes (first week) following infarction are elevation of the R-T interval above the iso-electric line; a convex, dome-shaped, or sloping R-T segment; the tendency of changes in level to be in opposing directions in Leads I and III, and in Lead II an appearance of the R-T segment simulating more or less closely those in Lead I or Lead III. In this early stage inversion of the T-wave often is absent or at most is diphasic in type. At a later stage, frank inversions of the T-waves appear and the T-waves are likely to be deep, abrupt and rather sharply peaked. In the reciprocal lead (Leads I and III act in a reciprocal manner) the T-wave is likely to become more positive, abrupt in ascent, and sharply peaked. At this stage, the R-T interval tends to return or does return to the iso-electric level. It is at this stage that the upward convexity of the R-T segment, preceding the sharply peaked inverted T-wave, presents the picture described by Pardee[9] as the "coronary T-wave."

In the light of these observations we have classified our electrocardiograms into types T_1 and T_3 and have subdivided these types into groups listed as typical, less typical, probable and indeterminate. That we cannot classify more of the tracings as typical is due to the fact that in many cases only a single electrocardiogram was taken and to the further fact that single or multiple electrocardiograms were taken in some cases at a long or indeterminate interval after infarction. Electrocardiograms obtained in cases of infarctions of about equal duration, in both the anterior and posterior portions of the left ventricle, may be difficult to classify into types T_1 or T_3.

Few reports of cases in the literature include a definite description of the site of infarction, an accurate study of the circulation in relation to the infarcted portion and the electrocardiographic tracings. Forty-seven cases in which necropsy was done at The Mayo Clinic, and in which inversion of the T-wave or alterations in the R-T interval were present, were studied. In these cases, the exact site of the infarction was observed especially with reference to the blood supply from the right or the left coronary artery. Of the forty-seven cases, twelve are selected for detailed report.

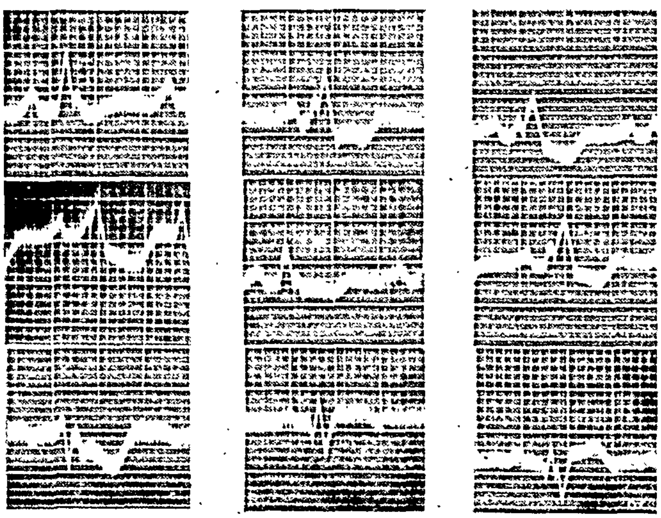
REPORT OF CASES

CASE 1.—A man, 57 years old, had complained of shortness of breath for seventeen months before he was first seen as a patient. Twenty-seven days before the first electrocardiogram was taken he had been seized with a feeling of pressure in his chest and had experienced much difficulty in breathing while driving his car. He had had to be helped to bed, had remained there three days, and two days more had passed before he had been able to walk about. After this, dyspnea had greatly increased. The blood pressure, measured in millimeters of mercury, was 130 systolic and 90 diastolic. In the first electrocardiogram there were inverted

T-waves in Leads II and III, suggestive of coronary occlusion. There was depression of the R-T interval in Lead I. The QRS interval was 0.12 second.

On the day of admission to the hospital the patient was unconscious for three or four minutes, and over the precordium he had heavy pressing pains which radiated into both arms. He was cold and clammy, and afterward became very weak. The following day there was a depressed R-T plateau in Leads I and II, with elevation of the plateau in Lead III. The T-wave appeared diphasic in all leads. Two days later, the R-T plateau had deepened in Leads I and II and had risen in Lead III. The QRS interval was 0.12 second. Although it was difficult to identify the T-wave with certainty, it appeared to be diphasic. The first electrocardiogram is of type T_3 and the last two tracings are of type T_1 (Fig. 5).

At necropsy an old infarct was found in the posterior surface of the left ventricle, in the area supplied by the right coronary artery. In the anterior surface of the left ventricle, in a region supplied by the anterior descending branch of the left coronary artery, there was a recent infarct.



A B C

Fig. 5.—Case 1. *A*, incomplete left bundle-branch block following infarction of the posterior portion of the left ventricle. The QRS interval is 0.12 second. *B*, incomplete right bundle-branch block one day after infarction in the anterior portion of the left ventricle; *C*, three days following infarction in the anterior portion of the left ventricle.

The history establishes accurately the time of occurrence of the two infarctions. The first electrocardiogram is associated with infarction in the posterior part of the left ventricle, whereas the last two are associated with infarction in the anterior portion of the left ventricle. The shift from an incomplete left bundle-branch block to an incomplete right bundle-branch block following the second infarction is significant. This case furnishes an explanation for electrocardiograms in which shifts in the type of changes in the T-wave occur and suggests that when such a shift is observed one must suspect the occurrence of infarction in a region of the left ventricle supplied by one coronary artery, together with preexisting infarction in a region supplied by the other coronary artery. This interpretation carries further weight if it is supported by a history of separate attacks indicative of coronary

occlusion, such as was obtained in this case. It is impossible to state the relative significance of infarction and bundle-branch disturbance in determining the contour and direction of the R-T intervals in this case.

CASE 2.—A man, 80 years old, came under observation because of an oppressive sensation in the chest, radiating to the left shoulder, which had begun about twelve hours previous to admission. He had been subject to attacks of paroxysmal dyspnea for eight years and to periods of oppression in the chest for four years.

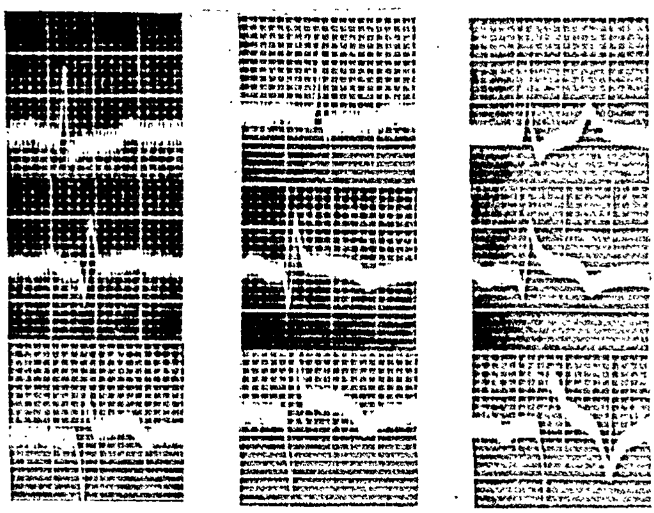
Fig. 6.—Case 2. *A*, recent infarction of the posterior portion of the left ventricle adjacent to the posterior interventricular septum; *B*, portion of posterior part of left ventricle folded back.

He became rapidly worse soon after admission to the hospital, leucocytosis and fever developed, and there was a fall in blood pressure from 110 systolic and 80 diastolic to 84 systolic and 52 diastolic. He died on the fourth day after admission.

At necropsy infarction involving most of the posterior surface of the wall of the left ventricle, the posterior portion of the interventricular septum, and one of the papillary muscles, was found (Figs. 6 and 7). This was shown to be due to occlusion of the right coronary artery. Purulent adhesive pericarditis was present.

Three normal electrocardiograms had been taken two and four years before the patient was admitted to the hospital. On the day of admission, there was a diphasic T-wave in Lead I, with depression of the S-T interval, and upright T-waves in Leads II and III, with elevation of the R-T interval. On the next day, the T-wave in Lead I became upright, but depression of the S-T interval remained. In Leads II and III, the T-wave had become inverted and the R-T interval had become an elevated plateau which arose high on the right limb of the wave. Similar but even more typical electrocardiographic changes of type T_3 were observed on the two following days.

CASE 3.—A man, 67 years old, had complained of attacks of precordial pain for fifteen years. He was admitted May 1, 1926, with a severe attack of precordial pain; the character of which, together with the results of physical examination,



A B C

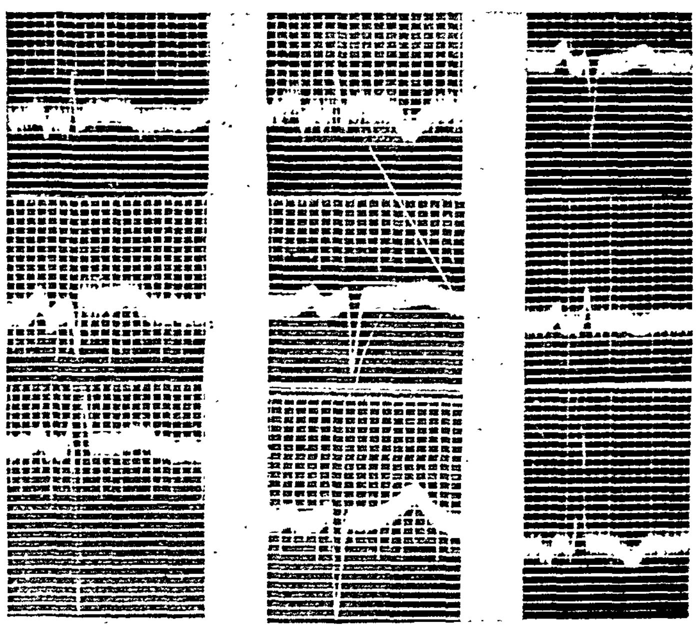
Fig. 7.—Case 2. Typical electrocardiogram of type T_3. *A*, an electrocardiogram made one day following the infarction in the posterior portion of the left ventricle that is shown in Fig. 6; the R-T interval is elevated in Leads II and III, and the S-T interval is depressed in Lead I. *B*, two days after infarction. *C*, three days after infarction; the origin of the R-T interval is high in Leads II and III; there is an abrupt, sharp, deep inversion of the T-wave in Lead III, and a sharp, high, positive T-wave in Lead I.

left no doubt but that we were dealing with a case of coronary occlusion with myocardial infarction. The blood pressure, which had been 130 systolic and 78 diastolic, now dropped to 95 systolic and 60 diastolic. From the third to the ninth day after infarction had occurred, the T-wave in Leads I and II became more positive and crescentic in contour; there was a gradual rise from the S-wave to the T-wave. Ten days after the infarction, the T-wave in Lead I was inverted, with a rounded, slightly positive wave preceding the T-wave; this contour frequently is seen preceding inversion of the T-wave in coronary occlusion (Fig. 8). At intervals of nineteen, twenty-one, twenty-four, twenty-six and forty-eight days after the coronary occlusion, the T-wave was inverted in Lead I. All of these tracings gave evidence of marked left ventricular preponderance. Two tracings, taken before the occlusion occurred, contained positive T-waves in all leads.

June 29, 1926, the patient had a second severe attack of precordial pain which lasted eight hours. Coronary occlusion was suspected but the evidence for it was

not conclusive. After eight days, he left the hospital. Tracings taken August 23, and 28, gave evidence of definite right ventricular preponderance with inversions of the T-wave in Leads II and III (Fig. 8). August 25, 1927, the patient was seized with a severe attack of precordial pain which lasted one day and which was indicative of myocardial infarction. Death occurred from progressive heart failure. Electrocardiograms taken at this time were unsatisfactory for technical reasons, and a positive opinion about the changes in the T-wave cannot be advanced.

There was sclerosis of the right coronary artery, graded 2. The anterior descending branch of the left coronary artery was markedly sclerosed, and its lower one-third was occluded. Infarction of the lower one-third of the anterior surface of the left ventricle and of the adjacent portion of the interventricular septum was found. There was marked thinning of the anterior and apical portion of the left ventricle,



A *B* *C*

Fig. 8.—Case 3. Electrocardiogram of type T_1 shifting to a less typical type T_3 in a case of old infarction in the apex and the anterior portion of the left ventricle. There was more recent infarction in the posterior surface of the left ventricle. *A*, tracing made ten days after first infarction; there is an elevated S-T interval in Leads I and II, with an upward convexity of the S-T interval. *B*, the features are the same as in *A* except for deeper inversion of the T-wave in Lead I, with typical reciprocal rise of the T-wave in Lead III; this electrocardiogram was made nineteen days after the first infarction. *C*, tracing made seven weeks after the second infarction; T waves are inverted in Leads II and III.

with an organized thrombus beneath this area. A region of healed pericarditis completely obliterated the pericardial sac; this probably was related to the history of pericarditis in childhood.

On the posterior surface of the heart, adjacent to the septum, midway between the apex and base, was an area about 5 by 4 cm., which in a tangential section had a distinctly yellowish cast but in which gross fibrosis was not present. A microscopic section taken from this region immediately adjacent to the septum showed that this area was undergoing infarction, with destruction of muscle fibers, with cellular infiltration and with practically no replacement by fibrous tissue. This was obviously a more recent infarct than the one at the apex, where the muscle fibers were practically all replaced by fibrous tissue. The infarction of the posterior basal portion of the left ventricle did not appear to have been acute, and it may

have occurred as long previously as June 29, 1926. If so, it would furnish a satisfactory explanation of the inversions of the T-wave in Leads II and III. The R-T interval in Lead III in these tracings had a rounded convexity somewhat suggestive of myocardial infarction.

CASE 4.—A man, 54 years old, had experienced substernal burning on exertion for seven years. Two and a half months before admission the patient had had an attack of substernal pain radiating down the left arm; pulmonary edema had appeared at this time. A similar attack had occurred three weeks later. The blood pressure at examination was 158 systolic and 112 diastolic.

At necropsy, sclerosis, graded 2, was found in the right coronary artery. In the left coronary artery sclerosis, graded 3, was found and the main trunk was occluded. There was chronic, diffuse fibrosis involving the anterior two-thirds of the left ventricle and the anterior half of the lower two-thirds of the interventricular septum. Fibrosis was found at the apex and in the adjacent posterior portion of the left ventricle. There was no fibrosis in the area supplied by the right coronary artery.

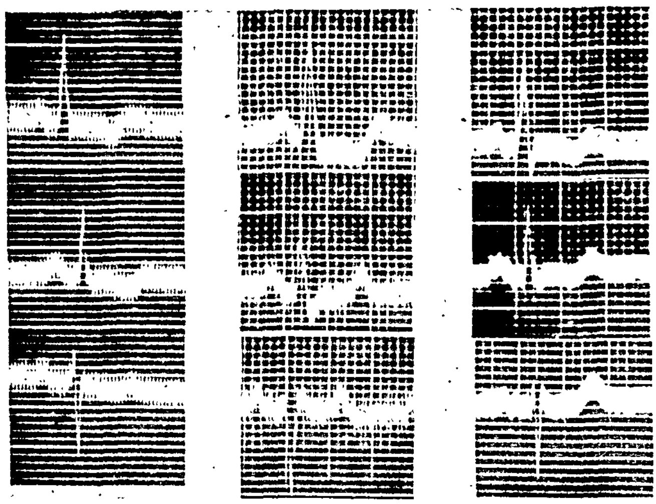


Fig. 9.—Case 4. Electrocardiogram made two-and-a-half months after infarction in the anterior portion of the left ventricle. *A*, there is a downward sloping R-T segment in Leads I and II and inverted T-waves in Leads I and II. *B*, four days later; there are depressed R-T segments in Leads I and II, and T-wave, in Lead I is diphasic. *C*, twenty-three days after tracing *A* was made: the tracing is the same as that in *B*; a sharply peaked, high T-wave has developed in Lead III.

The electrocardiogram taken the day of admission revealed inverted T-waves in Leads I and II with a downward sloping R-T interval in both leads. A tracing taken five days later disclosed upright T-waves in Lead II, although the R-T interval in that lead still had its origin below the iso-electric level. Essentially the same type of tracing was obtained twenty-three days after admission (Fig. 9). The T-wave in Lead III had a tendency to become more positive and more sharply peaked. The modifications of the R-T intervals observed here are sufficient to cause this tracing to be classified with those showing late changes of type T_1.

CASE 5.—A man, 58 years old, had an attack of acute dyspnea seven months before coming to the clinic following a heavy meal. There was a history of rheumatic fever at fifteen years of age, with an attack of pericarditis at that time, and of another attack at the age of twenty years. The patient had not complained of pain in the chest. At examination, the heart measured 21.5 cm. in its greatest transverse diameter, and there was a short to-and-fro murmur at the aortic area. The liver was markedly enlarged, and there was edema of the lower extremities. The blood pressure was 130 systolic and 70 diastolic. Death occurred suddenly while the patient was under treatment.

Midventricular infarct was observed anterior to the obtuse margin of the left ventricle. Dissection revealed that this region was supplied by terminal branches of the circumflex division of the left coronary artery or by the branches of the accessory anterior descending artery.

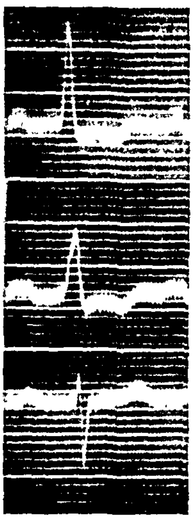


Fig. 10.

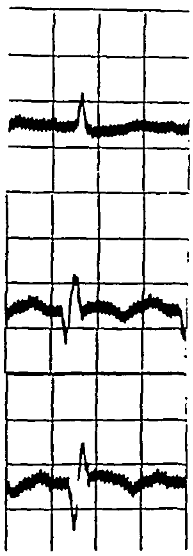


Fig. 11.

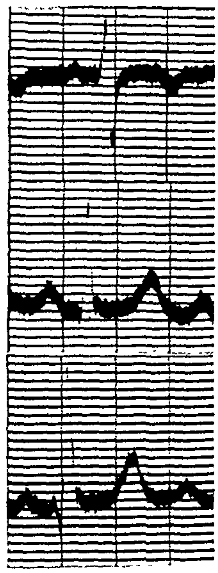


Fig. 12.

Fig. 10.—Case 5. The history suggested that infarction had occurred seven months before admission. There was old infarction in the anterior portion of the left ventricle. There are depression and slight upward convexity of the R-T interval in Leads I and II and diphasic T-waves in Leads I and II.

Fig. 11.—Case 6. Electrocardiogram made twenty days after the first attack suggesting infarction. There was infarction in the posterior surface of the left ventricle. The R-T interval in Leads II and III has a typical high origin and upward convexity.

Fig. 12.—Case 7. Electrocardiogram made in a case of old infarction in the anterior portion of the left ventricle. There is upward convexity of the S-T interval in Lead I, and high, sharply peaked positive T-waves in Leads II and III. This is a good example of the late type T_1.

In the electrocardiogram, taken twelve days before death, there was depression of the R-T level in Leads I and II, with diphasic T-waves in those leads. Slight rounding of the R-T interval was noted in each of these two leads. The contour and level of the R-T segment in Lead III appeared normal (Fig. 10).

CASE 6.—A man, 56 years old, had a severe attack of anginal pain, Nov. 24, 1927. The pain lasted for twelve hours, and morphine was required for relief. Dec. 3, 1927, the patient had another severe attack, this time with epigastric pain. He was taken to the hospital Dec. 6. At that time the blood pressure was 140 systolic and 90 diastolic. He died Dec. 25, 1927.

Necropsy revealed an acute infarct of the lower two-thirds of the posterior portion of the left ventricle, as well as infarction of the lower half of the posterior portion of the interventricular septum. There was considerable thinning of the posterior surface of the left ventricle. There was a small zone of infarction in the right ventricle, in a region closely adjacent to the posterior interventricular septum. The orifice of the right coronary artery was completely plugged by a thrombus which protruded from its orifice. In this particular case the right coronary artery supplied the posterior surface of the left ventricle as far to the left as the left or obtuse margin of the heart and extended inferiorly to the apex, as in Fig. 3. The infarcted areas were limited to the portion of the heart supplied by the right coronary artery.

The electrocardiogram, taken Dec. 13, disclosed inversion of the T-waves in Leads II and III, with the typical high origin and rounding of the R-T plateau seen in myocardial infarction (Fig. 11).

Case 7.—A man, 77 years old, came to the clinic because of incontinence of urine which proved to be due to carcinoma of the prostate. There was no history indicative of myocardial insufficiency, although the heart was moderately enlarged. The blood pressure was 154 systolic and 82 diastolic. Death followed suprapubic cystostomy for drainage of the bladder.

At necropsy there was a fairly well localized area of diffuse fibrosis in the anterior portion of the left ventricle and adjacent septum in the apical two-thirds of the heart. This region was found to be just distal to an area of calcification in the upper third of the anterior descending branch of the left coronary artery.

The electrocardiogram taken eleven days before death contained an inverted T-wave in Lead I, with slight upward convexity of the R-T segment (Fig. 12). There was no history indicating acute infarction of the myocardium, and the appearance of the infarcted region suggested that the infarction may have occurred gradually.

Case 8.—A woman, 64 years old, gave a history suggestive of angina pectoris of four or five years duration. Nov. 24, 1927, she had suffered from severe epigastric and precordial pain radiating down the left arm and was admitted to the hospital on the following day. At that time her blood pressure was 158 systolic and 86 diastolic. She became worse rapidly and died Nov. 30, 1927.

At necropsy, infarction was found involving the posterior surface of the left ventricle near the base. Regions of infarction also were discovered along the posterior interventricular sulcus, on what appeared to be the adjacent surfaces of the right and left ventricles; however, it was found that the posterior portion of the interventricular septum was abnormally placed, so that it encroached on the surface of the right ventricle. Consequently the region of infarction was practically confined to the posterior surface of the left ventricle and the adjacent part of the interventricular septum. The infarction was limited to the portion of the heart supplied by the right coronary artery.

The heart and vessels were injected with celloidin. Although there was some sclerosis of the left coronary artery, it could be seen that on the whole it was fairly well preserved (Fig. 13). The zone of infarction was shown by the areas in which blood vessels were not injected. It was also observed that the right coronary artery, although it had anastomotic connections with the left coronary artery through the abnormally situated interventricular septum, was not of sufficient caliber to nourish adequately the region which it supplied.

In the electrocardiogram taken two days after the patient's severe attack of angina pectoris, there was inversion of the T-wave in Leads II and III; also, the R-T interval took origin above the iso-electric level, and there was a tendency to convexity of the plateau preceding the T-wave. In Lead I, the R-T segment tended to originate slightly below the iso-electric level. The tracing on the second day following, exhibited the same characteristics, with minor variations. The R-T segment in Leads II and III was typical of that seen in myocardial infarction (Fig. 14). Death occurred two days after the last electrocardiogram was obtained.

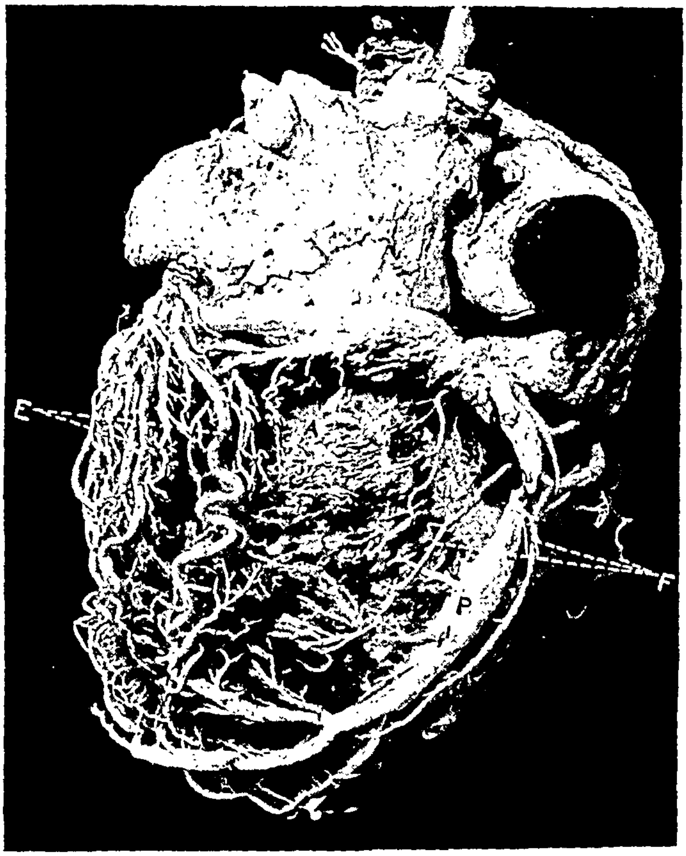


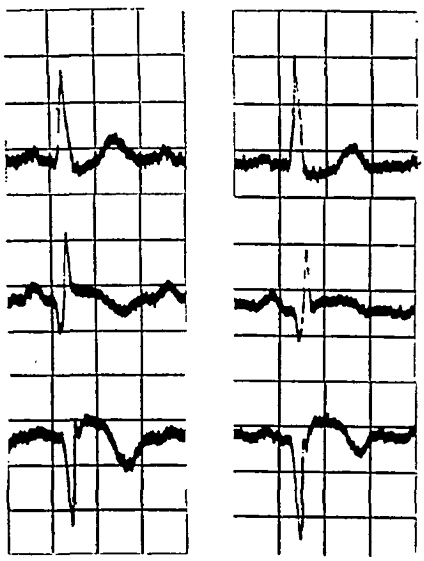
Fig. 13.—Case 8. Preparation, by celluloid-corrosion method, of a heart injected following occlusion of the right coronary artery. *A*, posterior surface of left ventricle in the region of infarction, showing the failure of the branches of the right coronary artery to be injected. *F*, branches of the right coronary artery; *E*, branches of the left coronary artery.

Case 9.—A man, 46 years old, had experienced much dyspnea following an acute respiratory infection one year before admission. During this year there had been varying degrees of cardiac decompensation, at one time requiring abdominal paracentesis. There was no history of pain in the chest. On entrance to the hospital, the patient presented the typical characteristics of marked cardiac decompensation. The blood pressure was 170 systolic and 130 diastolic. The patient failed to respond to usual measures. Death occurred from mesenteric thrombosis twelve days after admission.

At necropsy the apex of the heart was found to be the site of an old infarct, chiefly the aspect of the apex involving the posterior interventricular septum. An-

other old infarct was found 2 cm. from the base, at the juncture of the anterior interventricular septum and the anterior portion of the left ventricle, and measuring about 1 cm. in diameter. There was recent acute infarction in the posterior surface of the left ventricle and septum, extending from a point midway between the base and apex to within 1 cm. of the apex. Beneath this infarct, in its apical portion, a mural thrombus was found. This region of acute infarction, as well as the chronic infarction at the apex, was found to be in the distribution of the posterior descending branch of the right coronary artery.

Electrocardiograms were taken one and four days after admission. In the first tracing, the R-T interval was slightly depressed and ended in a diphasic T-wave in Lead I. In Leads II and III the R-T interval came off above the iso-electric level and the T-wave rose gradually to end in a summit. In the second tracing, the R-T level in Lead I was



A B

Fig. 14.

Fig. 15.

Fig. 14.—Case 8. *A*, electrocardiogram made two days after occlusion of the right coronary artery. There was infarction in the posterior surface of the left ventricle. The R-T interval is elevated in Leads II and III and the S-T interval is depressed in Lead I. *B*, electrocadiogram made four days after occlusion. The S-T interval in Leads II and III shows more pronounced upward convexity.

Fig. 15.—Case 9. Electrocardiogram made in a case of recent acute infarction in the posterior portion of the left ventricle. The R-T segment is slightly depressed in Lead I and slightly elevated in Leads II and III.

depressed and ended in an inverted T-wave. The elevation of the R-T segment in Lead II was less than in the first tracing and the peak of the T-wave was not so high. The elevation of the R-T interval and the high peaked positive T-wave in Lead III persisted (Fig. 15).

Such a tracing may be difficult to classify in its proper type, unless it is kept in mind that in the early stages, particularly, the classification must be made on the basis of whether Lead I or Lead III presents alterations in the R-T interval similar to those in Lead II. Furthermore, it is important to remember that early in the process of infarction the T-waves may become more positive rather than inverted. On

this basis it is probable that this tracing should be classified as one of type T_3. Change in the level of the R-T interval and the inversion of the T-wave in Lead I may have come from one factor or from a combination of three factors. Depression of the level of the R-T interval is to be expected with infarction in the posterior surface of the left ventricle. The inverted T-wave may have been a relic of preponderant left ventricular strain due to hypertension, of the effect of chronic infarction in the apex and the anterior portion of the left ventricle, or of both these factors. Had further electrocardiograms been made, it would have been possible, probably, to make a more accurate analysis of the changes in the R-T interval in relation to infarction. However, it can be said that the major changes in the R-T segments in Leads II and III

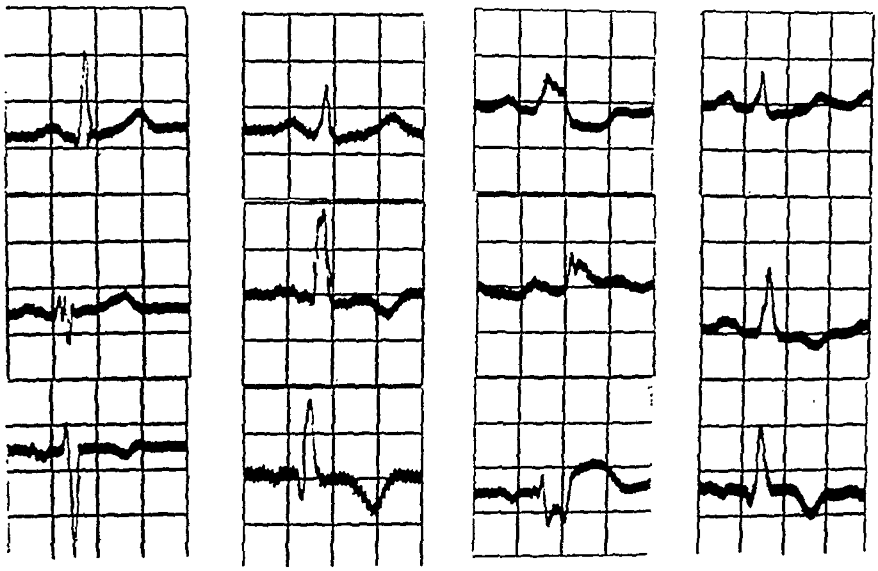


Fig. 16.—Case 10. Electrocardiograms taken *A*, before occlusion; *B*, thirty-six hours after acute infarction of the posterior portion of the left ventricle. The R-T interval in Leads II and III has a rounded contour. There is an exaggerated inverted T-wave in Lead III. *C*, incomplete bundle-branch block recorded on the day following the second infarction in the anterior portion of the left ventricle. *D*, tracing made five days after acute infarction. The R-T interval is elevated in Lead III and depressed in Lead I.

coincided with the more recent infarction in the posterior portion of the left ventricle.

Case 10.—A man, 58 years old, came to the clinic because of precordial and substernal pain. He had been in extreme ill-health with hyperthyroidism for seven years, until thyroidectomy had been performed five years before the admission for the pain in the chest. Psychosis of three months' duration had followed this operation. The patient had been subject to definite attacks of angina pectoris for three years, and in one of these attacks he had fallen on the street. An electrocardiogram taken the day of his admission was essentially normal. The day following admission he had a seizure of excruciating thoracic pain, with features typical of coronary occlusion. The pain lasted for about ten hours and was followed by elevation in temperature, fall in blood pressure, and leucocytosis. An electrocardiogram was

taken thirty-six hours after the onset of symptoms of occlusion. The alterations of the R-T interval in Leads II and III, and its depression in Lead I (Fig. 16), led to an ante-mortem diagnosis of coronary occlusion, with infarction in the posterior portion of the left ventricle, in the region supplied in the average heart by the right coronary artery. Four days after his first attack the patient had a prolonged attack of pain suggesting further infarction. Following this, the electrocardiogram gave evidence of incomplete right bundle-branch block. On the basis that the right bundle-branch usually receives its chief blood supply from the anterior descending branch of the left coronary artery, this electrocardiographic abnormality led us to suspect that occlusive changes were occurring in the anterior descending artery or its branches.

At necropsy a thrombus was found in the right coronary artery just before the posterior descending branch was given off. The major acute infarction was in the posterior portion of the left ventricle and septum, extending practically to the apex. Minor acute infarction was observed in the anterior and septal portions of the left ventricle about 1 cm. from the apex. In the right and left coronary arteries there was sclerosis graded 3.

Case 11.—A man, 58 years old, gave a history of having had an acute respiratory infection six weeks before admission. This had been followed by a wheezing cough, with pain over the anterior and posterior part of the chest. Following this, marked dyspnea had been noted, and for four or five weeks before admission the patient had been unable to lie down because of the dyspnea. Swelling of the lower extremities had been present for four weeks. On admission, the patient presented the general picture of congestive cardiac failure. The blood pressure was 176 systolic and 108 diastolic. The response to treatment was fairly prompt, but the patient was admitted in a similar condition one month later. Failure was gradual during the following six days, and death occurred from congestive cardiac failure and renal insufficiency.

At necropsy sclerosis, graded 2+, was found in the right coronary artery and in the left coronary artery, sclerosis, graded 3 was found. There was a small, old infarct at the juncture of the anterior portion of the ventricle with the septum, 1 cm. from the apex. A second chronic infarction was seen 2 cm. from the anterior interventricular sulcus and 2 cm. from the base. This was a wedge-shaped area 1 cm. in diameter, with its apex toward the endocardium. At the obtuse margin, in a region supplied jointly by the circumflex and the terminal branch of the right coronary artery, was a small amount of scattered fibrous tissue.

The electrocardiogram taken three months before death and eighteen days after the first admission of the patient, showed inversion of the T-wave in Leads I and II, with slight depressoin of the R-T segment in both leads (Fig. 17). This tracing was classified as probably of type T_1, chiefly because the changes in the R-T segment in Lead II resembled the characteristics formed in Lead I, whereas the R-T level in Lead III was unaltered. (Compare Fig. 17 with Fig. 5.)

Case 12.—A man, 54 years old, had had hypertension for ten years with a blood pressure ranging from 190 to 200 systolic. Four months before admission he had had an attack of severe dyspnea with a dull, aching pain in the precordium, which had lasted several hours and after which shortness of breath had been a prominent symptom. Eleven days before admission he had been seized with a sudden, sharp, knife-like pain in the precordium which had radiated down the lateral surface of the left arm as far as the elbow. There had been associated pallor, dyspnea, and

weakness. Relief had been obtained with morphine and nitroglycerine. Following the attack, his physician had found a low pulse pressure. The blood pressure on admission was 160 systolic and 140 diastolic. Death occurred from cerebral embolism the origin of which was an intracardiac thrombus at the apex of the left ventricle.

Sclerosis of the right and left coronary arteries, graded 2, was found. There was marked chronic and acute infarction of the anterior portion of the left ventricle, in its lower two-thirds, and of the anterior portion of the interventricular septum. There was marked thinning of the ventricle near the apex, with an organized thrombus underlying this area. This infarction was all in the region supplied by the anterior descending branch of the left coronary artery.

In the first electrocardiogram, made twelve days after the last severe seizure of precordial pain, the T-waves were diphasic in Leads I and II. On the following day, the T-wave was inverted in Lead I and

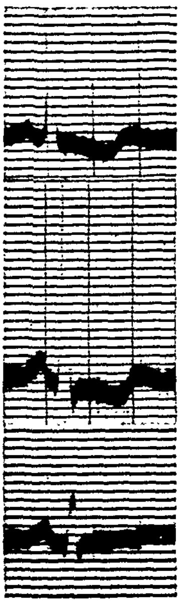
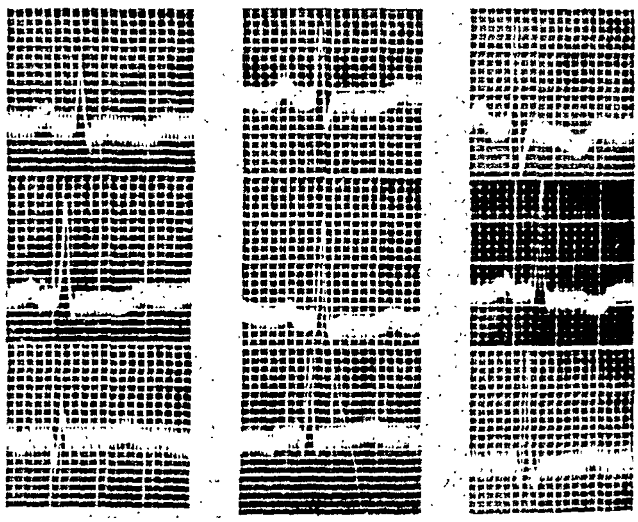


Fig. 17.



A B C

Fig. 18.

Fig. 17.—Case 11. Electrocardiogram of old infarction in the anterior portion of the left ventricle. The S-T interval is depressed in Leads I and II. There is a sloping S-T interval in Lead I and slight upward convexity in Lead II.

Fig. 18.—Case 12. *A*, electrocardiogram of old acute infarction in the anterior portion of the left ventricle, made twelve days after the last severe precordial pain and four months after the first attack of pain. The S-T interval in Lead I is rounded. The S-T interval in Leads I and II is slightly depressed. *B*, six days later; there are diphasic T-waves in Leads I and II. *C*, record made eight days after the first tracing. There is a downward sloping, slightly rounded S-T interval in Lead I.

diphasic in Lead II. In both leads, the R-T segment arose below the iso-electric line and in Lead I there was a slight upward convexity of the R-T segment. Six days later, the T-waves were inverted in Leads I and II and the R-T segment was typical of myocardial infarction. Death occurred eleven days after the last tracing was made (Fig. 18).

COMMENT

In the tabulation the cases have been divided into the types described. Study of these data shows that in twenty-one cases in which the electrocardiograms were definitely, less typical, or probably of

type T_1, the infarction occurred in the anterior and apical portion of the left ventricle, in the region supplied by the left coronary artery in the average heart. In six cases in which the electrocardiograms were of type T_3 infarction was found in the posterior portion of the left ventricle, the region supplied by the right coronary artery in the average heart. In four cases in which the electrocardiograms were of type T_3 and in one in which it was of type T_1, infarcts were found in both the anterior and posterior portions of the left ventricle.

In Case 3 the type of electrocardiogram which had been classified as type T_3 shifted to type T_1. It could be definitely established, in this case, that the old infarction was in the posterior portion of the left ventricle, in the region supplied by the right coronary artery and that the recent one was in the anterior surface of the left ventricle, in the region supplied by the left coronary artery.

In Cases 5 and 6 the type shifted from T_1 to T_3, with infarction in the anterior and posterior portions of the left ventricle. The older infarction in Case 5 occurred in the anterior portion and apex of the left ventricle. The probability is suggested that a similar condition existed in Case 6. Electrocardiograms showing curves of type T_1 or T_3 only, in patients with infarction in both the anterior and posterior portions of the left ventricle, probably indicate, according to the type present, the region in which infarction was more recent or more progressive. At any rate, successive electrocardiograms showing a definite shift from one type to another must lead to the strong suspicion that infarction has occurred in both the anterior and posterior portions of the left ventricle; and further, the latest type of change which occurs in the R-T interval usually will indicate the portion of the left ventricle in which the more recent or more extensive infarction has occurred.

In one case in a single electrocardiogram a curve was found that was classified as of a "less typical" type T_3 but the infarction was found to be in the anterior portion of the left ventricle. Cases such as this require further electrocardiograms before a definite opinion as to the type may be ventured. In the remaining cases the electrocardiograms could not be grouped according to types, and their correlation with the region of infarction in the left ventricle is not possible at present.

In these patients the most frequent site of infarction was in the region supplied by the anterior descending branch of the left coronary artery. The left coronary artery alone was responsible for infarction in twenty-five cases and the right coronary artery in eleven. However, including those cases in which infarction occurred in both the anterior and posterior portions of the left ventricle, we found the left coronary artery at fault in thirty-six cases and the right in twenty-two. These figures emphasize the fact that infarction in the portion of the left ventricle supplied by the right coronary artery is much more common than ordinarily is supposed.

This study indicates that an electrocardiogram of type T_1 is associated with infarction of the anterior portion of the left ventricle in the region supplied by the average left coronary artery. An electrocardiogram of type T_3 was found to be associated with infarction in the posterior portion of the left ventricle, in the region usually supplied by the right coronary artery. Parkinson and Bedford concluded that "all available evidence points to the fact that it is occlusion of the left coronary artery or its branches which produces characteristic T-waves of infarction." They recognized that infarction of the posterior surface of the left ventricle occurred when the right coronary artery was occluded, but they did not associate with its occlusion any changes in the T-wave characteristic of infarction. So far as we know, the present study is the first in which attention has been called to the fact that occlusion of the right coronary artery, producing infarction in the posterior portion of the left ventricle, causes characteristic changes in the R-T interval. Furthermore, so far as we know, this is the first study in which it is pointed out that changes in the R-T interval in infarction of the regions of the left ventricle that are supplied, in the average heart, by the right and left coronary arteries, respectively, are distinctly different and characteristic.

Our experience agrees with that of Parkinson and Bedford in that we found that gross infarction of the right ventricle was extremely rare. We have discussed elsewhere some probable anatomical explanations for this. Infarction of the right ventricle was found in only four cases of twenty-two in which occlusion of the right coronary artery or its branches was the source of injury. The infarction of the right ventricle in each case was minimal in amount and was closely adjacent to the injured posterior interventricular septum. In Case 12, in which the right coronary orifice was plugged by a thrombus, all of the right ventricle except a small area adjacent to the septum escaped infarction; this is not easily explained.

The electrocardiographic changes observed by Smith, in dogs, do not parallel the phenomena found by us in the human being following infarction. This is probably accounted for if one examines the difference between the distribution of the coronary arteries to the left ventricle of the dog[2, 8] and of man. In the dog the circumflex branch of the left coronary artery is much more important than in the average heart of human beings and supplies the posterior portion of the left ventricle and the interventricular septum. This region is supplied by the right coronary artery in the human heart, and infarction of this area in the human being was found to produce an electrocardiogram of type T_3. Smith did not discover significant changes in the T-wave on ligation of the right coronary artery in dogs, probably because the posterior surface of the left ventricle escaped infarction due to the fact that the right coronary artery did not supply this region.

In the study[1] of the effect of strain exerted predominantly on one ventricle, the conclusion was reached that strain predominantly of the left ventricle tended to cause inversion of the T-waves in Lead I or Leads I and II, whereas strain predominantly on the right side of the heart tended to cause inversion of the T-waves in the combined Leads II and III. Thus, as far as effect on the T-waves is concerned, infarction of the anterior portion of the left ventricle acts in the same general direction as strain predominantly of the left ventricle and infarction in the posterior portion of the left ventricle in the same direction as strain predominantly of the right ventricle. In the cases considered here there were nineteen of definite hypertension, in which electrocardiograms were of the type T_1 in fifteen. Inasmuch as hypertension produces inversion of the T-wave in the same leads as those in which inversion of the T-wave is observed in infarction of the anterior portion of the left ventricle, it cannot be denied that hypertension may have contributed in some measure to the T-waves observed in these cases. Hypertension does not determine the type of changes in the T-wave when infarction occurs in the posterior surface of the left ventricle. This was shown by the fact that in two cases of hypertension in which infarction in the posterior portion of the left ventricle was found, the changes in the R-T interval were of T_3 type. In a third case in which the electrocardiogram was of T_3 type, there was infarction in both anterior and posterior regions of the left ventricle. In one case there was an R-T interval of a less typical type T_3 which could not be explained on the basis either of hypertension or of infarction in the anterior portion of the left ventricle.

In seven cases there probably had been preexistent hypertension. In three of these cases there were changes in the R-T interval of type T_1, and in each case infarction was present in the anterior portion of the left ventricle. In four cases there were changes in the R-T segment of type T_3 and in each of these, infarction was found in the posterior part of the left ventricle.

In one case of aortic stenosis there was a change in the R-T interval of type T_1, and infarction of the anterior portion of the left ventricle was present. On the other hand, in a case of syphilitic aortitis and aortic regurgitation, presenting change in the R-T segment of type T_3 infarction in the posterior portion of the left ventricle was found.

Thus it appears that strain predominantly on one ventricle does not determine changes in the T-wave when this strain is competing with infarction. Furthermore, infarction, if it occurs in a region in which its effect on the T-wave is opposite to that of strain predominantly on one ventricle, the infarction will determine the form and direction of the changes in the R-T segment.

THEORETICAL CONSIDERATION

Elsewhere we have discussed the possible meaning of the observation that different portions of the left ventricle give rise to electrical effects acting in different directions on the T-wave. We pointed out that these results suggested that so far as effects on the T-wave were concerned, the left ventricle might be conceived of as being divided by a plane corresponding roughly with the line of division between the regions of the ventricle supplied by the right and the left coronary arteries in the average heart; and further, judging from their similar effects on the T-wave, the evidence at hand suggested that the posterior portion of the left ventricle acts on the T-wave in the same general direction as does the right ventricle. If this observation is correct, we suggest that it is not necessary to assume that the relatively small mass of muscle of the right ventricle alone produces electrical effects balancing those of the larger left ventricle.

It is probably more than a coincidence that this plane of division in the left ventricle follows the average plane of separation between the blood supply derived, respectively, from the right and from the left coronary arteries. However, it seems likely that it is the site of the area of infarction in the left ventricle rather than any particular blood supply that determines the changes in the R-T interval.

This leads to a consideration of the effect of the base and apex on the formation of the T-wave. Our results indicated that infarction confined to the apex produced changes of type T_1. When infarction of the anterior surface of the left ventricle and anterior septum was combined with infarction of the apex, the same type of change resulted. Infarction of the apex, together with infarction of the posterior region of the left ventricle produced a change of type T_3. In cases 16 and 27 there was infarction in the middle part of the ventricle with changes of type T_1, although in neither case could the electrocardiographic changes be said to be entirely typical of infarction. The area of the heart which produces electrical effects differing from those produced by the apex includes the right half of the basal two-thirds of the posterior surface of the left ventricle, but when the apex is involved in infarction, along with the latter area, the direction of the changes in the R-T interval is not determined by the apex. On the basis of their effects on the T-wave, it seems reasonable to assume from a study of these cases that the left ventricle may be divided into an anterior two-thirds including the apex, and a posterior *one-third*; this seems more reasonable than to consider the apex and base as exerting differential effects.

The anatomical architecture of the ventricular muscle as described by Mall, particularly the arrangement of the layers in the posterior surface of the left ventricle (Fig. 19) and their relation to the blood

supply, needs further study. Such study may help explain why the anterior and posterior portions of the left ventricle produce electrical effects acting in different directions.

It is impossible to state with certainty the mechanism of production of the normal T-wave in the electrocardiogram. It seems fairly certain that the T-wave is associated with the termination of the refractory period in the muscle fibers of the two ventricles. Katz and Weinman have concluded that the normal T-wave is due to the asynchronous cessation of electrical activity in the fractionate components of the ventricular muscle. The work of Wilson and Herrmann, as interpreted by Lewis, indicated that the T-wave is the resultant of electrical forces

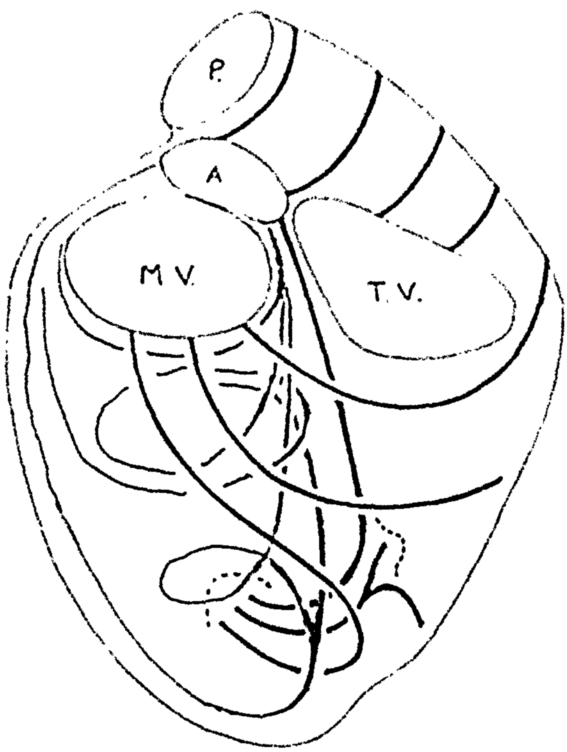


Fig. 19.—Posterior aspect, showing diagrammatically the arrangement of the chief muscle groups in the human heart. The sinospiral muscle group is in black and the bulbospiral in gray. The sinospiral muscle group, besides being distributed to the right ventricle, makes up a part of the basal three-fifths of the posterior portion of the left ventricle and of the interventricular septum in the region supplied by the average right coronary artery. *P*, pulmonary artery; *A*, aorta; *M.V.*, mitral ring; *T.V.*, tricuspid ring.

in the two ventricles and in that sense is a bicardiogram; and Lewis further interprets their investigations to mean that the upright T-wave in Lead I is predominantly a right ventricular effect, and the upright T-wave in Leads II and III is predominantly a left ventricular effect. The changes in the R-T interval observed in these cases are best explained when considered in the light of the conclusions of both of these investigations.

The various alterations of the R-T segment in myocardial infarction have as their common feature a deviation from the iso-electric level.

Careful study of these alterations shows that opposite effects often are observed in the early and in the later stages of infarction. In the first few days after infarction the R-T wave usually rises above the iso-electric level; it may have an upward convexity, or it may rise to a summit in a T-wave at the end of the plateau. In the course of a few days, or at most in two or three weeks' time, the level of the R-T segment returns to or below the zero level, and the T-wave becomes inverted. This strongly suggests that the initial alteration of electrical effects in the infarcted area differs from the later alterations. Finally, the R-T segment usually returns to normal, and the inversion of the T-wave disappears; this change requires months and sometimes one to two years for its completion.

It is impossible to discuss the mechanism involved in the effect of infarction on the R-T interval without a knowledge of the effect of infarction on conduction time and duration of electrical activity of the muscle fibers in the area involved. It is likely that these effects will be found to be, in the first few days after infarction, different and probably opposite from those occurring subsequently. It seems reasonable to assume that the effects on the R-T interval in infarction are the result of alterations in the electrical activity of the area of the infarct and that the resultant of electrical forces which produce the normal R-T interval are disturbed. Furthermore, it is reasonable to assume that when there is infarction of one portion of the ventricle, the electrical activity in the relatively uninjured portion and in the opposite ventricle occurs in the same direction as before. The solution of the problem of alterations in electrical effects in infarcted cardiac muscle will contribute greatly to a knowledge of the exact mechanism in the production of the inverted T-waves and, by inference, to better understanding of the factors responsible for the upright T-wave.

SUMMARY AND CONCLUSIONS

1. The importance of a study of infarction in relation to the distribution in the left ventricle of the right and left coronary arteries has been pointed out.

2. The branches of the arteries which supply the left ventricle, whether they originate from the right or the left coronary artery, are similar in architecture.

3. It has been shown that in the distribution of the right coronary artery in the right ventricle, branches leave the main artery in the same general plane as that of the branch from which they arise, whereas, in the left ventricle, they leave the coronary artery at right angles and penetrate directly through the myocardium.

4. Myocardial infarction of the right ventricle is rare.

5. Infarction which follows occlusion of the right coronary artery or its branches almost always is found in the posterior portion of the

left ventricle and septum and at times in the apex. The area that becomes infarcted depends on the distribution of the right coronary artery in the left ventricle.

6. Occlusion of the left coronary artery usually involves its anterior descending branch, although occasionally the circumflex branch is the site of occlusion. In occlusion of the anterior descending branch, infarction at the apex and in variable portions of the anterior portion of the left ventricle and septum are the rule.

7. Infarction of the left ventricle produces characteristic changes in the R-T segment of the electrocardiogram. The essential change is considered to be the fact that the R-T interval fails to establish an isoelectric level. From a study of the electrocardiogram, the changes usually can be classified as of types T_1 and T_3 as suggested by Parkinson and Bedford.

8. Infarction limited to the anterior portion of the left ventricle, either alone or combined with infarction of the apex, or infarction of the apex alone, produces modifications of the R-T segment of type T_1, whereas infarction of the posterior portion of the left ventricle, with or without infarction of the apex, produces modifications of the R-T interval of type T_3.

9. In cases in which infarction occurred in both areas at successive intervals of time, there was a corresponding shift in the changes in the R-T segment, and the last change observed corresponded with the last portion undergoing infarction.

10. On the basis of its effects on the R-T wave of the electrocardiogram, the left ventricle may be conceived of as being divided by a plane on either side of which the electrical forces which produce the R-T interval act in different directions. Apparently this plane of division in the left ventricle corresponds roughly to the usual line of division between the distribution of the right and left coronary arteries. Results of a previous investigation indicated that right ventricular strain was associated at times with inversion of the T-wave in Leads II and III. Inasmuch as these are the two leads in which occurred the chief changes in the R-T interval and, later, inversions of the T-wave in cases of infarction of the posterior portion of the left ventricle, it is suggesetd that in the posterior region of the left ventricle the electrical effects on the T-wave act in the same direction as those in the right ventricle.

11. It is suggested that the infarcted portion acts as a unit with reference to the remaining relatively normal fibers and that in the infarcted region there is some disturbance of the normal activation of the muscle fibers or of the duration of their electrical activity. Physiologic experiment determining whether fibers of the infarcted area

emerge from the refractory stage late or early as compared to the relatively normal fibers may throw some light on the mechanism of the alteration of the R-T wave.

12. So far as this study goes, the results indicate that typical alterations of the R-T interval in infarction of the left ventricle are characteristic in type and enable one to localize the region involved. The identification of the region involved usually will indicate which coronary artery is the seat of trouble.

TABULATION

CLASSIFICATION OF ELECTROCARDIOGRAMS ACCORDING TO TYPES

	SITE OF THE INFARCTION IN RELATION TO THE CORONARY ARTERIES			
	CASES	LEFT CORONARY ARTERY	RIGHT CORONARY ARTERY	BOTH
Typical types				
T_1 or T_3				
T_1	5	4		1
T_3	5		3	2
T_1 to T_3	1			1
T_3 to T_1	1			1
Less typical types				
T_1 or T_3				
T_1	10	10		
T_3	5	1	2	2
T_1 to T_3	1			1
T_3 to T_1				
Probable types				
T_1 or T_3				
T_1	7	7		
T_3	1		1	
T_1 to T_3				
T_3 to T_1				
Indeterminate types				
T_1 or T_3				
T negative in Leads I, or in I and II	2	1*	1†	
T negative in Leads III or in II and III	1		1†	
Inverted T in Leads I, II, III	1		1	
Bundle-branch block				
Complete or incomplete right	6	2	2	2
Complete or incomplete left	1			1

*T waves diphasic in Leads I and II and iso-electric in Lead III.
†Tracing lost.

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THE AGE AND SEX INCIDENCE OF ARTERIAL HYPERTENSION*

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IT HAS often been stated that essential hypertension† is found most frequently among middle-aged and pre-elderly individuals. In only a few instances, however, have the statements been accompanied by statistics. Similarly, although the condition has been said to be more common among men than among women, the basis for establishing this as a fact has not been presented.

There are few data available that concern directly either the age or the sex incidence of hypertension. However, a number of contributions appear in the literature, which contain reference to the ages of patients who were presented as illustrations of various aspects of hypertension or sphygmomanometry. Tables I-A—I-E compare the results of some of these investigations calculated and arranged according to the percentage of patients in different age periods.

These reports have been separated into four groups as follows: A, hypertension as found in different periods of life; B, age of patients with hypertension at time of death; C, life insurance statistics; D, E, hospital reports. This classification is necessary for a discussion of the age incidence of hypertension because each group possesses characteristics which make it difficult to compare one group with another.

HYPERTENSION AS FOUND IN DIFFERENT PERIODS OF LIFE

Early Childhood.—Amberg[1] reported 25 instances of increased blood pressure found in children from six to sixteen years of age. Nine of these cases were in all probability of the essential hypertension type, and four of the nine had no detectable renal involvement. These 9 cases are not included in Table I-A because of the rarity of hypertension in early childhood. There are other instances given in the literature of hypertension in children, but the increase in blood pressure was probably secondary to a coexisting nephritis.

Hypertension in Youth.—There are three significant reports concerning blood pressure examinations of persons from sixteen to forty years of age. The investigators have usually considered 140 mm. Hg to be the dividing line between a normal and an abnormally high systolic blood pressure. Alvarez[2] in a report of the blood pressure

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†The term "essential hypertension" is used to define persistent high blood pressure in the larger circulation due to other causes than primary genitourinary disease.

readings of about 260 drafted men showed that 141 had a systolic pressure above 140 mm. Hg. If a calculation is made in terms of the percentage of frequency with which the individuals fall into various age groups (Table I-A), it is found that there is a close approximation

TABLE I-A

THE RELATIVE FREQUENCY WITH WHICH THE DIAGNOSIS OF HYPERTENSION IS MADE AT VARIOUS PERIODS OF LIFE*

AGE	Alvarez (2)		Alvarez, Wulzen, Mahoney (3)				Diehl, Sutherland (4)		Wildt (9)		Bowes (10)		Richter (11)	
	Total cases examined 263 Men	Cases of hypertension 141 Men	Total cases examined 6,000 Men	Cases of hypertension 1,245 Men	Total cases examined 8,934 Women	Cases of hypertension 246 Women	Total cases examined 5,122 Men	Cases of hypertension 586 Men	Total cases examined 248 Both sexes	Cases of hypertension 101 Both sexes	Total cases examined 50 Men	Total cases examined 100 Women	Total cases examined 165 Both sexes	Cases of hypertension 83 Both sexes
90–									1.6	1.	8.0	3.0		
85–90									5.6	8.9		7.0	9.1	10.8
80–85									16.1	14.9	22.0	16.0	14.5	15.7
75–80									23.	20.8	28.0	24.0	31.5	31.3
70–75									27.4	25.8	20.0	29.0	21.2	22.9
65–70									15.7	18.8	22.0	21.0	17.6	15.7
60–65									10.5	9.9			6.1	3.6
35–40	28.1	28.3	1.2	1.	2.5	9.3	0.3	0.2						
30–35	36.1	36.2	2.2	1.5	4.5	7.7	0.9	0.7						
25–30	1.9	1.4	8.9	7.4	10.4	6.9	6.5	5.1						
20–25	19.8	21.2	39.3	39.1	30.4	25.2	33.6	35.7						
15–20	14.1	12.8	48.6	51.	52.	50.8	58.8	58.2						

*Calculated and arranged in terms of percentage of total diagnoses occurring in each age group.

between the age distribution of the 141 cases of hypertension and the total 263 cases whose systolic blood pressures were recorded. Alvarez, Wulzen, and Mahoney[3] have reported the blood pressure readings of 14,934 college freshmen, both men and women. The age distribution of

the 1245 men with hypertension was very similar to that of the entire 6,000 men examined. Of the 8,934 women who were examined, 246 had a systolic pressure of 140 mm. Hg or over. The age distribution of the women with high blood pressure ran parallel with that of the entire group except between the ages of thirty-six and forty years where there was an actual as well as a relative increase in the frequency of individuals with hypertension. Diehl, and Sutherland[4] have presented a similar investigation on the blood pressures of 5,122 college men. Here again the age distribution of the 586 men with increased blood pressure was similar to that of the entire group.

These investigators have found hypertension to be surprisingly common among young men. Considering all the men examined, regardless of age, Alvarez found hypertension in 53.6 per cent of drafted men; Alvarez, Wulzen and Mahoney found it in 20.7 per cent of male college freshmen; while Diehl and Sutherland found it in 11.5 per cent of men in the first year of college. This frequency becomes more striking when hospital statistics are considered which include persons from youth to senility. The latter type of investigations showed hypertention to exist in 9.6 per cent (Obuch Institut für Gewerbekrankheiten, Moskau[5]) and 9.7 per cent (Universitäts Klinik, Kiel[6]) of the male patients examined.

Alvarez, Wulzen and Mahoney found hypertension in 2.8 per cent of the young women they examined. The hospital statistics mentioned above demonstrated hypertension to be present in 7.9 per cent[5] and 25.9 per cent[6] of the total number of women examined.

The three investigations on hypertension in youth possess one common characteristic, namely, that the examinations were made on normal individuals in whom there was no reason to suspect ill health. Moog and Voit[7] have reported 16 instances of hypertension in patients between sixteen and twenty-eight years of age, and Magniel[8] has presented 3 similar cases. These patients differed from those discussed above in that they suffered from ill health and their hypertension required treatment.

Hypertension in Old Age.—Wildt[9] reported the blood pressure readings of 248 patients between sixty and ninety-six years of age, 101 of whom had systolic blood pressures of over 150 mm. Hg. Forty-seven per cent of the cases of hypertension and 50 per cent of the total patients examined were between seventy and seventy-nine years of age. The age distribution of the cases with hypertension was similar to that of the entire group. Bowes[10] determined the blood pressure of 100 women and 50 men above sixty-four years of age, the majority of whom had hypertension. The distribution of the men, according to five year age periods, showed the greatest incidence between seventy-five and seventy-nine years of age. The same calculation for the women showed the period of maximum incidence five years earlier

than in the men. Richter[11] observed the blood pressure in 165 elderly individuals between the ages of sixty and eighty-nine years, 83 of whom had a systolic pressure of 150 mm. Hg or more. The greatest

TABLE I-B

THE RELATIVE AGE DISTRIBUTION OF PATIENTS WITH HYPERTENSION, AT THE TIME OF DEATH*

AGE	Shaw (12)	Bell and Hartzell (13)				Bell, Clawson (14)
	Cases of hypertension 47 Both sexes	Total cases examined 1,529 Men	Cases of hypertension 120 Men	Total cases examined 542 Women	Cases of hypertension 23 Women	Cases of hypertension 417 Both sexes
80–90		5.8	9.2	5.2	13.	2.4
70–80	8.					11.5
60–70	16.	16.1	27.5	12.1	13.	27.6
50–60	20.	23.9	40.8	17.9	34.8	32.9
40–50	32.	20.1	13.3	18.3	26.	16.3
30–40	12.	20.5	8,3	19.6	13.	6.7
20–30	6.	13.5	0.8	26.9		1.9
10–20						0.7

*Calculated and arranged in terms of percentage of total diagnoses occurring in each age group.

age incidence occurred in the seventy-five to seventy-nine year group. The curve for the age distribution of hypertension among the 83 individuals closely approximates that for the age distribution of the entire group of 165 persons.

AGE INCIDENCE OF HYPERTENSION AT TIME OF DEATH

Hypertension may be an indirect cause of death. Presumably the high blood pressure in the cases to be discussed (Table I-B) had existed for some time before death; nevertheless, the patients show a wide distribution of ages. Shaw[12] studied the clinical histories and post-mortem findings of 50 cases in which the systolic blood pressures were above 150 mm. Hg. The heaviest incidence was found in the forty to forty-nine year age group. No control figures were given. Bell and Hartzell[13] have recorded the results of 2071 necropsies including 120 men and 23 women who had had hypertension. These patients with hypertension varied from twenty-one to ninety years of age. The greatest incidence of the cases was for patients between fifty-one and sixty years of age. Bell and Clawson[14] have reported 420* autopsies on patients with hypertension who ranged from thirteen to ninety years of age. In 184 instances the diagnosis of hypertension was made on the basis of the post-mortem weight of the heart. Sixty per cent of the patients with hypertension were between the ages of fifty-one and seventy years of age. The decade from fifty-one to sixty years showed the greatest number of cases of hypertension.

LIFE INSURANCE STATISTICS

Large life insurance companies require a medical examination of each applicant. From time to time there has been presented information based on the results of these examinations. These reports do not include the results of all the examinations, because the data for those applicants accepted for life insurance have usually been separated from those for individuals who were rejected because of physical ailments. As a result of this, life insurance statistics on hypertension possess certain peculiarities. Were it possible to combine the data obtained from these two sources, the result would still fall short of representing a cross-section of the physical condition of the community, because those who apply for life insurance represent for the most part individuals who believe themselves to be in perfect health. From this comparatively healthy group of applicants the medical examiners weed out those whose blood pressures are abnormally high as well as those who show some of the complications of hypertension and whose prognosis, therefore, is unfavorable. Furthermore, old age is in itself a handicap to acceptance for life insurance, and as a result there are few figures for persons above sixty-five years of age.

The accepted risks, therefore, represent a selected group of persons with hypertension under sixty-five years of age. These selected individuals usually have only moderately elevated blood pressures and no complications. The rejected risks include only a portion of the remaining cases of hypertension in the community, for elderly individ-

*The ages of 417 patients were recorded.

uals and those who know themselves to be suffering from hypertension or other ailments rarely present themselves for life insurance. The importance of this division of cases is illustrated by the figures of Van Wagenan,[15] which show 5.7 per cent of the accepted individuals and

TABLE I-C

THE RELATIVE FREQUENCY OF HYPERTENSION AS SHOWN BY LIFE INSURANCE STATISTICS*

AGE	Fisher (16)		Fisher (19)	Symonds (17)				Frost (20)		Dublin, Fisk, Kopf. (21)		Rogers, Hunter (22)	AGE
	3156 Accepted risks with hypertension	1274 Risks rejected because of hypertension	4165 Risks rejected because of hypertension	Total accepted risks 150,419 Men	Cases of hypertension 8,579 Men	Total accepted risks 11,937 Women	Cases of hypertension 422 Women	Total cases examined 146,992 Both sexes	Cases of hypertension 2,568 Both sexes	Total accepted risks 16,662 Men	Cases of hypertension 1,199 Men	4,214 Accepted risks with hypertension	
90													90
80													80
70									7.				70
				1.3	6.7	0.3	1.7	1.	11.			28.2	
60	8.6 8.9	16.7 14.7	35.9	2.4	10.3	1.4	12.1	2.	15.	6.6	21.		60
	18.4	22.		4.9	14.5	3.2	16.1	7.	17.	18.2	25.5		
50	33.2	26.	28.7	8.6	17.8	7.3	27.3	10.	13.			33.4	50
	31.1	20.4		12.2	15.4	9.8	19.9	15.	10.	34.8	26.5		
40			17.5	15.4	12.4	13.2	11.1	18.	8.			38.4	40
				17.9	9.7	17.2	6.4	18.	7.	35.3	23.5		
30			17.8	18.4	7.7	22.6	3.3	16.	7.				30
				13.9	4.6	19.8	1.7	9.	3.	5.2	3.4		
20				4.8	0.8	5.3	0.5						20
10													10

*Calculated and arranged in terms of percentage of total diagnoses occurring in each age group.

22.5 per cent of the declined persons to be between fifty-six and seventy years of age. The "declined risks" were refused insurance because of various ailments. Fisher's figures[16] show the ages of those individuals who were refused life insurance solely because of ele-

vated blood pressure. In his series 31.4 per cent of the rejected candidates were between fifty-four and sixty years of age, while only 17.5 per cent of the accepted individuals fell into this same age group.

Although there is evidence to show that the age at which hypertension is most likely to occur is not the same in both men and women, the life insurance reports do not always indicate the sex of the applicants. Judging from the figures of Symonds[17] over 90 per cent of the applicants are men.

Many life insurance companies instruct their medical examiners to consider that hypertension exists if there occurs a persistent systolic pressure of 15 to 20 mm. Hg above the average for persons of the same age and sex; other companies consider 139 mm. Hg to be the upper limit of normal systolic blood pressure regardless of the age or sex of the individual. These figures are perhaps a little lower than those considered by many internists to indicate hypertension. So far as it is known, there is no universally accepted dividing line between normal and high blood pressure. Osler[18] in his *Practice of Medicine* sets the dividing line at 160 mm. Hg, and this is a figure which is in common use, although in childhood and early youth lower blood pressure would be considered as abnormal. At the present time more attention is being paid to the diastolic pressure than formerly. A patient may be considered to be suffering from hypertension who has a diastolic pressure in the neighborhood of 100 mm. Hg, even though the systolic pressure is only moderately elevated.

The accepted individuals recorded by Fisher[16] show their greatest incidence to be between the ages of forty-five and forty-nine. On the contrary, the rejected persons had the peak of their age incidence between fifty-four and sixty years of age. A later report by the same author[19] concerning only rejected cases shows essentially the same age distribution as the previously rejected individuals. The figures for the men and the women were not separated in this report, and no control figures were given.

Symonds[17] analyzed the blood pressure readings of over 162,000 accepted risks and found 8,579 men and 422 women with systolic pressures over 140 mm. Hg. The significance of this figure as the dividing line between normal and abnormally high blood pressure is shown by the fact that of this group there were only 704 men and 38 women whose pressures were above 150 mm. Hg and only 372 men and 22 women with systolic readings above 155 mm. Hg. Symonds showed the greatest incidence of those individuals whose pressures were above 140 mm. Hg to occur between forty-five and forty-nine years of age in both men and women, with a relatively higher incidence among women in the five years preceding this age group.

Frost[20] has presented 2,568 cases of hypertension which were discovered through the medical examinations of 146,992 applicants for life

insurance. Many of the cases with known cardiovascular or renal disease were not included in the group with hypertension. The cases of hypertension occurred in both sexes, the individuals ranging from fifteen to seventy years of age. The graph presented by Frost from which the data in Table I-C were approximated shows a gradual rise in the incidence of hypertension, reaching a maximum in the fifty to fifty-four year age period and slowly falling off thereafter.

Dublin, Fisk and Kopf[21] have reported statistics on 16,662 male policy holders including 1,199 men with hypertension. These authors found hypertension in 5.5 per cent of the policy holders between thirty-five and forty-four years of age and in 23 per cent of the "accepted risks" who were more than fifty-five years old. There were, however, relatively few elderly policy holders, and as a result the greatest number of persons with hypertension were found to be between thirty-five and forty-four years of age.

Rogers and Hunter[22] noted that of 4,214 accepted cases of hypertension, the greatest incidence occurred in individuals between forty and forty-nine years of age. The men and women were considered together and no controls were presented.

HOSPITAL REPORTS

This group consists of reports from various hospitals in Europe and America and includes patients ranging from ten to eighty-nine years of age (Table I-D).

Weitz[23] reported 64 instances of hypertension discovered in the Medical and Nerve Clinic at Tubingen. The fifty-six to sixty year group contained the largest number of cases.

Gelman[5] has presented the blood pressures of 3,761 patients from the Obuch Institut für Gewerbekrankheiten, Moskau. These cases included 255 men and 89 women whose systolic blood pressure was above 140 mm. Hg. The greatest incidence of hypertension among the men occurred in those between forty and forty-nine years of age with only slightly fewer in the succeeding decade. These twenty years accounted for 60 per cent of the total number of men whose blood pressures were elevated. Over 75 per cent of the women with hypertension were between thirty and forty-nine years of age, and a majority of these individuals were between thirty and thirty-nine years old.

The ages and blood pressures of over 4,000 patients of the Universitäts Klinik at Kiel have been recorded by Saller.[6] These included 232 men and 453 women whose systolic pressures were greater than 143 mm. Hg. The maximum age incidence for hypertension in both men and women occurred between the ages of fifty-one and fifty-nine The distribution among the younger age groups was quite different in the two sexes; about 27 per cent of the male and 10 per cent of the female patients with hypertension being less than forty-two years of age.

Hypertension in this series of patients appeared at an earlier age among men than among women.

Eighty-one cases of "malignant hypertension" have been collected by Keith, Wagener and Kernohan[24] from the Mayo Clinic. In all save

TABLE I-D

THE RELATIVE FREQUENCY OF HYPERTENSION AS SHOWN BY HOSPITAL REPORTS*

AGE	Weitz (23)		Gelman (5)				Saller (6)				Keith et al (24)		AGE
	Total cases examined 359 Both sexes	Cases of hypertension 64 Both sexes	Total cases examined 2,641 Men	Cases of hypertension 255 Men	Total cases examined 1,120 Women	Cases of hypertension 89 Women	Total cases examined 2,385 Men	Cases of hypertension 232 Men	Total cases examined 1,743 Women	Cases of hypertension 453 Women	Cases of hypertension 48 Men	Cases of hypertension 33 Women	
90													90
80													80
70							3.9	13.3	5.2	14.9			70
	11.4	21.8											
	14.7	23.4	0.7	2.			8.	21.1	7.9	19.8	2.1	3.	
60	23.9	34.3									4.2	0.	60
	20.3	15.6	8.7	27.8	3.1	10.1	13.3	23.7	16.9	33.8	14.6	24.3	
50	29.5	4.7									27.1	18.2	50
			20.9	32.5	12.6	30.3	16.8	15.2	18.9	22.	18.7	21.2	
40											18.7	12.1	40
			31.2	19.6	34.2	47.2	24.4	14.2	23.1	6.2	6.2	9.1	
30											4.2	3.	30
			33.6	14.1	45.5	11.2	20.7	9.9	17.1	2.4	0.	3.	
20			4.7	3.9	4.5	1.1		2.6		0.7	2.1	6.1	20
							13.5		10.9		0.	0.	
10											2.1	0.	10

*Calculated and arranged in terms of percentage of diagnoses occurring in each age group.

one of these cases the systolic pressure was above 220 mm. Hg. In both sexes hypertension occurred with considerable frequency after thirty years of age, the maximum incidence being in the forty to forty-nine year group.

BOSTON CITY HOSPITAL RECORDS

The data about to be presented have been derived from the records of both the wards and the out-patient department of the Boston City Hospital. It is necessary to consider the statistics from each of these

TABLE I-E

THE AGE INCIDENCE OF HYPERTENSION, AS FOUND IN THE BOSTON CITY HOSPITAL*

AGE	Out-patient Department				Hospital Wards			
	Controls 606 Men	Cases of hypertension 442 Men	Controls 607 Women	Cases of hypertension 1,170 Women	Controls 831 Men	Cases of hypertension 499 Men	Controls 447 Women	Cases of hypertension 574 Women
90–95							0.5	0.2
85–90		0.3		0.1	0.1	0.6	0.5	0.2
80–85		1.1		0.3	1.	1.8	1.	0.5
75–80	1.5	3.6	0.2	1.5	1.3	3.	3.1	3.5
70–75	4.	6.5	0.8	3.2	4.	6.8	3.4	7.9
65–70	4.1	16.3	2.1	9.3	5.9	14.9	6.1	11.
60–65	6.1	25.5	4.8	17.7	6.9	18.8	9.4	18.8
55–60	7.9	10.6	5.4	16.5	10.6	15.4	8.3	13.6
50–55	12.	16.9	8.7	17.9	10.9	12.8	7.6	18.3
45–50	9.9	6.7	10.9	17.3	10.	8.4	7.4	8.5
40–45	10.	5.4	10.7	8.1	8.9	7.6	6.9	6.3
35–40	9.1	2.3	13.7	5.3	9.4	3.4	6.9	5.6
30–35	7.1	1.8	9.5	1.8	8.8	2.6	9.6	2.8
25–30	6.1	0.9	9.5	1.	9.2	1.8	9.	1.7
20–25	7.9	0.9	9.2	0.	7.2	1.2	10.5	0.7
15–20	8.2	0.9	7.9	0,3	3.6	0.6	6.9	0.
10–15	5.9		6.4		2.4	0.2	2.9	0.5

*Calculated and arranged in terms of the percentage of total diagnoses which occurred in each five-year age group.

sources separately, for they represent different clinical types of patients. The majority of those patients who entered the wards for treatment were seriously ill, and if they had hypertension, they were suffering in the majority of instances from one or another of the major

complications of this condition. The out-patient cases of hypertension, on the other hand, occurred in relatively healthy individuals and usually without complications.

From April, 1925, until December, 1928, inclusive, 1620 diagnoses of hypertension were made in the medical out-patient department. The age of eight of the patients was not recorded. A few of the individuals considered they were well and were examined to determine if ill health existed. The rest of the patients submitted themselves for examination because of symptoms which did not prevent them from walking to the hospital. Seldom were patients discovered to be so seriously ill as to make it desirable for them to enter a hospital ward.

The blood pressure of all patients was taken by the auscultatory method using the Riva-Rocci type of sphygmomanometer with a 12.5 cm. cuff. The diagnosis of hypertension was made by the various members of the staff. An analysis of the blood pressure readings of 1600 of the total number of cases showed that the systolic pressures were 160 mm. or over in 91.6 per cent, and in only 3.1 per cent were the systolic readings less than 150 mm. Hg. The diastolic pressures were less frequently elevated; 66.1 per cent of the cases had a diastolic pressure of 100 mm. Hg or more, and in 85.9 per cent it was 90 mm. Hg or more. These cases of hypertension may be said to have been of two classes: those in which the systolic pressure was only moderately elevated, but in which the diastolic reading was in the neighborhood of 100 mm. Hg; and second, those in which both the systolic and diastolic pressures were considerably elevated.

Of the total group of out-patient cases, 281 or 17.3 per cent exhibited evidence of impaired kidney and cardiac function or cerebral hemorrhage. In a number of patients special studies were made in order to determine if any complications existed. These tests included electrocardiographic tracings, nonprotein nitrogen determinations on the blood and various renal function tests.

During the three years 1925-1927, 1104 patients with hypertension entered the wards. The age of 31 patients was not determined. Seven hundred and twenty or 65.2 per cent had a disorder of the heart, kidney or brain. Thus, there was a much higher incidence of complications among the ward cases than among the out-patient cases with hypertension. The medical services contributed 90.3 per cent of the total cases and the neurological and surgical services contributed 4.4 per cent and 3.5 per cent respectively. The few remaining cases were reported from the gynecological, obstetrical, dermatological, pediatric and aural services.

The blood pressures of the ward patients with hypertension tended to be higher than the out-patient cases. The systolic blood pressures in 95.3 per cent of 300 consecutive ward cases were 160 mm. Hg or more, and only 2.7 per cent of these cases had a systolic pressure of less than

150 mm. Hg. The diastolic pressures also were elevated in a large percentage of the cases, in 82 per cent it was 100 mm. Hg or over. Fifty-five per cent of the ward cases had systolic pressures of 200 mm. Hg or over, while only 33 per cent of the out-patient cases had systolic pressures of the same magnitude.

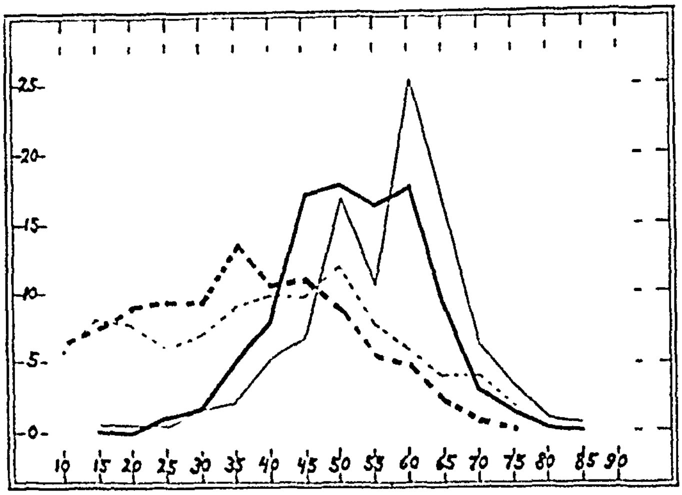

Fig. 1.—Graphic presentation of age incidence of out-patients with hypertension with that of the clientele of the Out-Patient Department of the Boston City Hospital. The abscissa represents the age period in years, the ordinate the percentage of the total number of cases. The male patients with hypertension are represented by the thin continuous line, the female patients by the thick continuous line. The control male cases are represented by the thin interrupted line, the control female cases by the thick interrupted line.

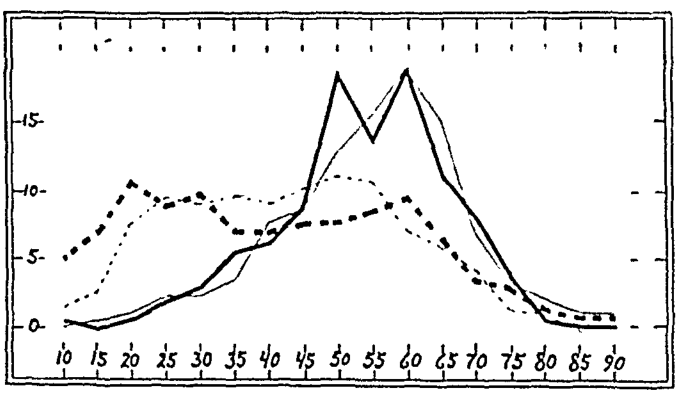

Fig. 2.—Graphic presentation of age incidence of ward patients with hypertension with that of the clientele of the medical wards of the Boston City Hospital. The abscissa represents the age period in years, the ordinate the percentage of the total number of cases. The male patients with hypertension are represented by the thin continuous line, the female patients by the the thick continuous line. The control male cases are represented by the thin interrupted line, the control female cases by the thick interrupted line.

Table I-E and Figs. 1 and 2 show the percentage frequency with which hypertension was found at various ages. The figures are arranged in terms of the percentage of cases which occurred in each five year age group. A few cases were found in individuals between twelve and twenty years of age, but hypertension did not occur with a frequency

above 10 per cent in the five-year groups below forty years of age. After the age of seventy the incidence of hypertension dropped quite sharply. Among women the condition occurred earlier in life than in the men. This was especially evident in the out-patient cases where the curve for the incidence among women showed a rise a full five years before there was a similar rise for the men. More than half the cases

TABLE II

INCIDENCE OF HYPERTENSION AT DIFFERENT AGES CONTRASTED WITH THAT FOR THE CLIENTELE, BOSTON CITY HOSPITAL

AGE	MEDICAL OUT-PATIENT DEPARTMENT				HOSPITAL WARDS			
	Hypertension 1612 Cases		Control 1213 Cases		Hypertension 1073 Cases		Control 1278 Cases	
	Men 442	Women 1170	Men 606	Women 607	Men 499	Women 574	Men 831	Women 447
10-14			36	39	1	3	20	13
15-19	4	4	50	48	3	0	30	31
20-24	4	0	48	56	6	4	60	47
25-29	4	12	37	58	9	10	76	40
30-34	8	20	43	58	13	16	73	43
35-39	10	62	55	83	17	32	78	31
40-44	24	95	61	65	38	36	74	31
45-49	30	201	60	66	42	49	83	33
50-54	75	209	73	53	64	105	90	34
55-59	47	193	48	33	77	78	88	37
60-64	113	207	37	29	94	108	57	42
65-69	72	107	25	13	74	63	49	27
70-74	29	37	24	5	34	45	33	15
75-79	16	18	9	1	15	20	11	14
80-84	5	4			9	3	8	5
85-89	1	1			3	1	1	2
90-94					0	1	0	2

occurred in patients whose ages were not over twenty years apart: 69.3 per cent of the male out-patient department cases occurred in patients between the ages of fifty and sixty-nine years of age, while 69.4 per cent of the females were between forty-five and sixty-four years of age inclusive. Among the ward patients with hypertension 61.8 per cent of the males and 61.7 per cent of the females were between fifty and sixty-nine years old. Up to fifty years of age there was little difference in the percentage age frequency curve for the two sexes, but after this age the frequency of hypertension in women increased more rapidly than in men.

It is necessary to compare the age distribution of these cases of hypertension with the ages of patients treated for other conditions. In order to do this there has been tabulated in Tables I-E and II the ages of the 1213 persons who were examined in the medical out-patient department during the month of March, 1929, and the ages of 1278 individuals who were admitted to the medical wards of the hospital during the months of April, August and December, 1927.

In the medical out-patient department 54.3 per cent of the male controls and 12.2 per cent of the male patients with hypertension were less than forty-five years old, while 66.9 per cent of the female controls and 16.4 per cent of the women with hypertension were of similar age. In the wards about 50 per cent of the controls and about 17 per cent of the patients with elevated blood pressure were less than forty-five years of age.

Figs. 1 and 2 show the curves for the age distribution of both control patients and patients with hypertension plotted in terms of the percentage of cases occurring in each five-year age period of life. The curve for women tends to be of the plateau type, while that for men shows a definite peak in the sixty to sixty-four year age group. Examination of the curves for hypertension shows two striking incisures, one in that for the male out-patient cases and the other in that for the female ward cases, both occurring in the fifty-fifth to fifty-ninth year group. If the age incidence is arranged for ten-year periods, as has been done in some of the reports discussed above, these incisures disappear. This might be interpreted to signify that five-year periods are too short for statistical significance. When the total cases are separated into two groups, the one representing uncomplicated hypertension and the other representing cases complicated by chronic nephritis, chronic myocarditis, or cerebral hemorrhage, age frequency curves are obtained essentially like those presented in Figs. 1 and 2.

RELATIVE FREQUENCY OF HYPERTENSION IN MEN AND WOMEN

Most writers on hypertension are of the opinion that hypertension is more frequently found among men. Table III is based upon all the data which we have found available on this subject. There are several reports in the literature on various aspects of hypertension and sphygmomanometry which have been based on analyses of fairly large groups of individuals. In Table III we have calculated the relative number of men and women with hypertension presented in each of these reports.

The relative incidence of hypertension found in the two sexes must necessarily have been influenced by the comparative numbers of men and women who presented themselves for examination. For example, Symonds[17] reported the blood pressure readings of over 162,000 holders of life insurance policies. Since 92.6 per cent of all these cases were men, it is not surprising to find that over 95 per cent of those discovered to have hypertension were of the male sex.

The determination of the relative frequency with which hypertension occurs in the two sexes should be based on the comparative frequency with which men and women with high blood pressure are found as a result of examining equal numbers of each sex. Wherever possible, we have attempted to reproduce this ideal situation by calculating what

TABLE III

SEX INCIDENCE OF HYPERTENSION

SOURCE		TOTAL CASES EXAMINED			CASES OF HYPERTENSION				
								Corrected for Sex Incidence in Total Cases	
		Total Cases	Per Cent Men	Per Cent Women	Total Cases	Per Cent Men	Per Cent Women	Per Cent Men	Per Cent Women
Gibes	(26)		Not Given		90	65.6	34.4		
Kulbs	(25)				288	59.7	40.3		
Keith, Wagener, Kernohan	(24)				81	59.3	40.7		
Cummings	(27)				150	44.0	56.0		
Bowes	(10)				150	33.3	66.7		
Alvarez, Wulzen, Mahoney	(3)	14,934	40.2	59.8	1,491	83.5	16.5	88.3	11.7
Bell and Hartzell	(13)	2,071	73.8	26.2	143	83.8	16.2	64.8	35.2
Symonds	(17)	162,356	92.6	7.4	9,001	95.3	4.7	61.9	38.1
Bell and Clawson	(14)	4,578	72.4	27.6	420	78.6	21.4	58.3	41.7
Gelman	(5)	3,761	70.2	29.8	344	74.2	25.8	54.9	45.1
Saller	(6)	4,128	57.8	42.2	685	33.8	66.2	27.2	72.8
Boston City Hospital			Control Cases						
O. P. D.	Total	28,906	47.8	52.2	1,620	27.8	72.2	29.5	70.5
Wards	Total	1,278	65.0	35.0	1,104	46.8	53.2	32.2	67.8
O. P. D.	Uncomplicated				1,387	23.9	76.1	25.7	74.3
Wards	Uncomplicated				384	39.9	60.1	26.3	73.7
O. P. D.	Complicated				233	47.3	52.7	49.5	50.5
Wards	Complicated				720	50.7	49.3	35.7	64.3

the result would be were the examination made in this manner. The results of these calculations appear in Table III under the column headed "corrected for sex incidence in total cases." As an illustration, let us again examine the data presented by Symonds.[17] As a result of the medical examination of this large group of accepted "life insurance risks," 8579 men (95.3 per cent) and 422 women (4.7 per cent) were discovered to have systolic blood pressures of 140 mm. Hg or over. The 162,356 "accepted risks" were made up of 92.6 per cent men and 7.4 per cent women. If these cases had been composed of equal numbers of each sex, there would have been 4,630 men with high blood pressure $(8579 \times \frac{50}{92.6})$ and 2850 women with hypertension $(422 \times \frac{50}{7.4})$. The cases with elevated blood pressures would then be made up of 61.9 per cent men and 38.1 per cent women.

The data of reports available in the literature show a wide variation in the relative frequency with which hypertension was found in the two sexes, regardless of whether one examines the actual number of hypertensives of each sex reported to have high blood pressure or whether one corrects the figures for the sex incidence shown by the total group examined. This variation may be due in part to the fact that the sources of these statistics are so different as to prevent ready comparison.

The medical out-patient records of the Boston City Hospital show a decided preponderance of female hypertensives over male. This is but slightly decreased when corrected for the relative numbers of men and women who make up the clientele of this section of the hospital. There were 28,906 control cases representing all the new patients who were admitted to the medical out-patient department during the forty-five months under consideration. The figures for the ward cases show hypertension to be more equally distributed between the two sexes, but when corrected for the sex incidence of the controls, the situation is found to be essentially the same as occurred in the medical out-patient department. The corrected figures from both of these sources showed that about 70 per cent of the cases of hypertension occurred in women while only about 30 per cent of the cases occurred in men. The figures of Saller[6] showed a similar sex distribution when calculated on the supposition that equal numbers of men and women were examined.

The Boston City Hospital cases can be separated into two groups: those complicated by chronic nephritis, chronic myocarditis, or cerebral hemorrhage; and those which showed none of these complications. When the statistics for the uncomplicated group are corrected according to the above method, it is found that 73.7 per cent of the ward cases and 74.3 per cent of the out-patient cases occurred in women. The group with complications showed the cases to be distributed more equally between the two sexes, but even here males do not predominate.

Arterial hypertension was present in 2.9 per cent of the total number of male patients, and in 6.6 per cent of the total number of female patients admitted to the medical out-patient department during the period under consideration.

The data presented above indicate that while high arterial blood pressure without functional or organic kidney damage may in rare instances be present in childhood, its occurrence among young adults is not an infrequent manifestation. The fact that the age incidence curve shows a sudden rise after the five-year period of forty-five to forty-nine in women and fifty to fifty-four in men, calls for special consideration. It has been suggested on the basis of morphological studies of the cardiovascular system (Janeway,[28] Volhard[29]), as well as on the basis of physiological observations (Weiss and Ellis[30]), that in the causation of high blood pressure increased peripheral resistance plays an important rôle. Suggestive evidence is also available that this increased resistance, at least in one group of patients, is caused by the contracted state of the arterioles (Ellis and Weiss[31]). The more exact mechanisms which lead to this increase in the peripheral resistance are not known at present, although clinical observations and experiments on animals clearly indicate that several mechanisms may be responsible for elevated arterial blood pressure.

The coincidence of a great increase in the occurrence of hypertension with onset of the involutionary changes in the body suggests a correlation between the two conditions. Two interpretations may be offered in explanation of this: (1) It is possible that high blood pressure exists symptomless in the same individuals in early life, but only with the onset of involutionary changes becomes manifest in symptoms and signs. (2) It is also possible that simultaneously with the onset of involution, changes occur in the organs, including those of internal secretion, which regulate the blood pressure. As a result the blood pressure becomes elevated.

Although it is certain that the first interpretation explains a number of cases, the available statistical data on groups of persons considered normal indicate that the age incidence does not increase essentially until the beginning of involution, when it increases markedly. The correlation between involution and high blood pressure, therefore, cannot be denied, although a more precise definition of the exact nature of this correlation cannot be offered at present.

SUMMARY AND CONCLUSIONS

1. The curve of age incidence of out-patient and ward patients with hypertension in the Boston City Hospital shows a gradual and progressive rise up to the age period of forty to forty-five years. After the age period of forty to forty-five there is a sudden rise in the curve. After the age of seventy, the incidence drops sharply. Over 60 per cent of

the cases occurred in patients between the ages of forty-five and sixty-nine inclusive.

2. The onset of the steep rise in the age incidence curve of hypertension occurs almost five years earlier for women forty-five to forty-nine years) than for men (fifty to fifty-four years).

3. Hypertension was present more frequently among female than among male patients of the Boston City Hospital. It occurred in 2.9 per cent of the total number of male, and 6.6 per cent of the total number of female patients admitted to the medical out-patient department during the period under consideration.

4. The fact that a sudden rise in the age incidence of hypertension occurs at a time in each sex which coincides with the age at which involution of the male and female glands of internal secretion and other organs begins, suggests the possibility of an etiological relationship between involutional changes of the human body and a group of patients with hypertension.

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THE DISTORTION OF THE ELECTROCARDIOGRAM BY CAPACITANCE*

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WHEN the General Electric Company first developed the amplifier tube as a method of recording the electricity of the heart, tests were made by H. B. Marvin of the General Engineering Laboratory

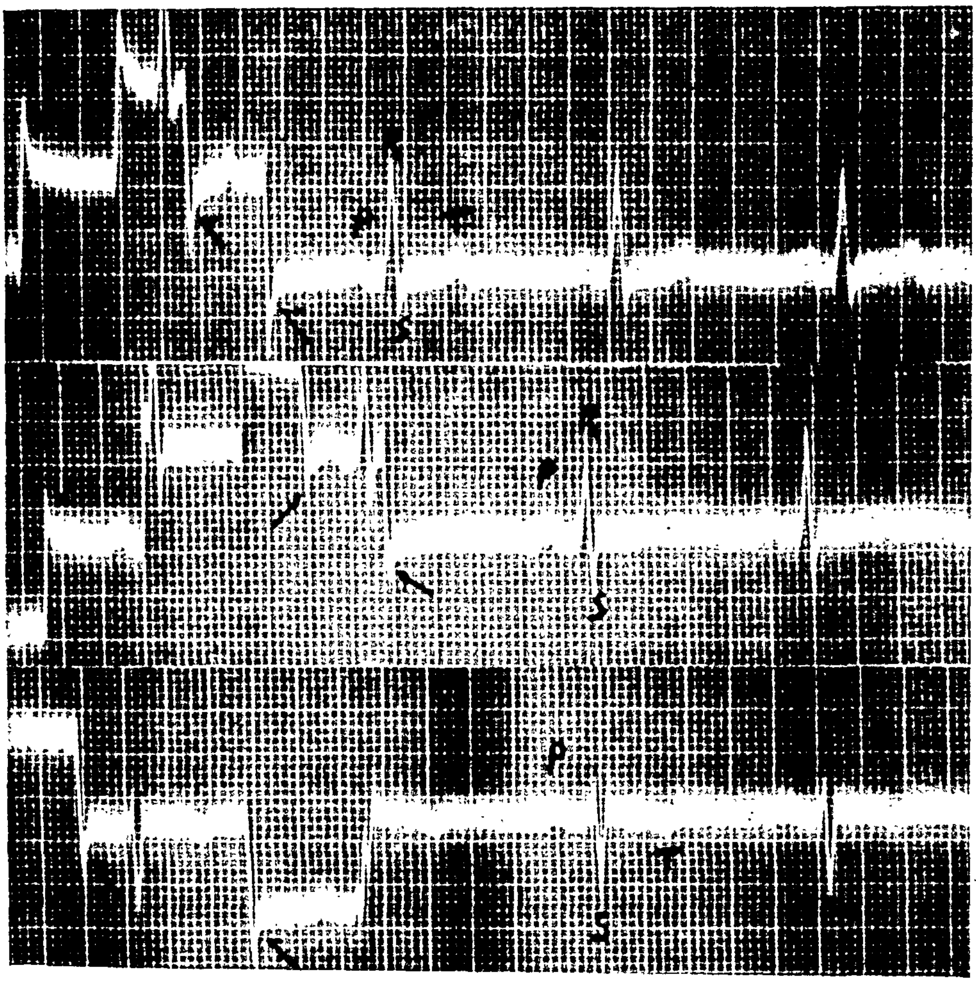

Fig. 1.—Record taken with the string galvanometer on a patient with high resistance. Comparing with Fig. 2, note the considerable overshooting at the test of standardization, the larger amplitude of QRS and T-waves than in Fig. 2.

of the General Electric Company, Schenectady, in conjunction with me, of the ability of this instrument to record the action current of the human heart. At the New York Hospital records were taken of

*From the Cornell University Medical School and the Second Medical Division of New York Hospital.

numerous patients, first with a large model of the Williams-Hindle electrocardiograph, and then with the instrument which had been devised in the General Electric Laboratory. These records were in all respects identical, and they were shown to the medical profession at the meeting of the American Medical Association at Atlantic City in June, 1925. Following this I had an opportunity to use one of these instruments before they were placed on the market, and my experience with it led me to believe that the records which it produced were identical with the records obtained from the same heart by the string

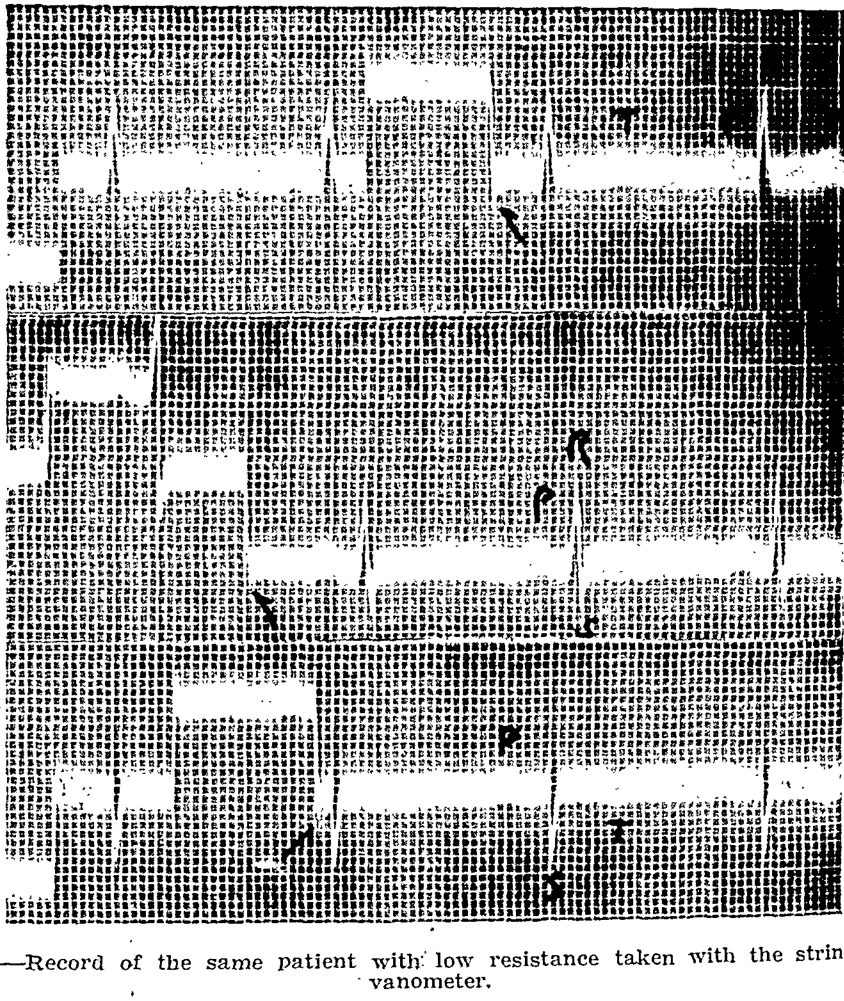

Fig. 2.—Record of the same patient with low resistance taken with the string galvanometer.

galvanometer type of instrument when the resistance of the patient was low. It was observed that with the amplifier tube instrument no distortion of the curve resulted from a high resistance of the skin of the patient, as occurred when using the string galvanometer. If a record was obtained from a patient by means of the string galvanometer, and owing to high skin resistance the overshooting was great, a record obtained from the same wires, without changing the electrodes but using the radio amplifier tube instrument, would show no evidence of overshooting.

Fig. 1 is the record of a patient taken with the string galvanometer. The resistance in the three leads, as measured by substitution, was 3900 ohms for Lead I, 5700 ohms for Lead II, and 7000 ohms for Lead III. It will be seen in the control of standardization that there is marked overshooting after the test current is applied, and it will be seen in the record that there is a distortion due to this. This record should be compared with Fig. 2 which was taken with the same instrument, with the resistance in all three leads 2000 ohms. There is but the slightest overshooting after the jump, due to the standardization test in this record, and the different appearance of the curve is evident;

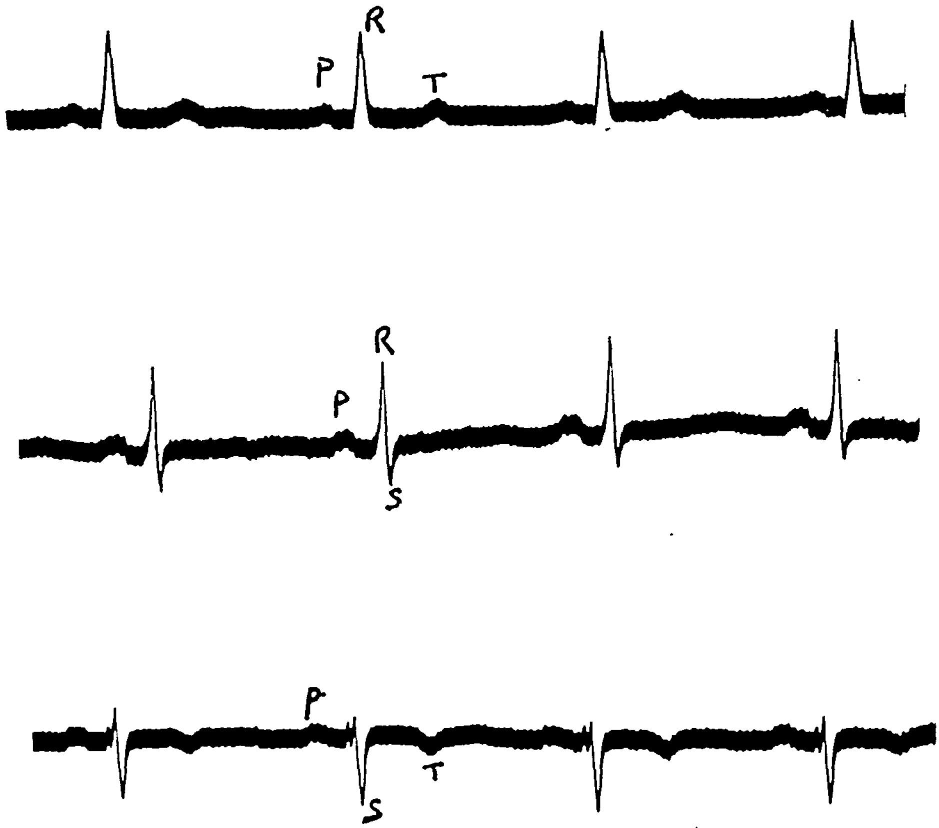

Fig. 3.—Record of the same patient taken with the amplifier tube electrocardiograph. Notice that the form of the waves is identical with that recorded in Fig. 2.

there is no S-wave in Lead I as is seen in Fig. 1; the amplitude of the R-wave is less in this lead, as is also the amplitude of the T-wave. Fig. 3 is a record taken from the same patient with the amplifier tube instrument immediately after the record in Fig. 1 was taken, and while the resistance of the patient was still high; the electrodes were not disturbed, but the lead wires were changed from one galvanometer to the other. It will be seen that this curve shows no evidence of distortion such as is seen in Fig. 1; it closely resembles Fig. 2. Fig. 4 is a record, taken with the string galvanometer, of another patient whose resistance was very high, Lead I measuring over 10,000 ohms, Lead II measuring 9000 ohms, and Lead III over 10,000 ohms. Fig. 5 is a record of

the same patient taken with the amplifier tube instrument as described above, immediately after Fig. 4 was obtained. It is seen that there is no evidence of overshooting in this record; the amplitude of the QRS group is less and is probably normal for this patient; the overshooting indicated at the point of the arrows in Fig. 4 is not present.

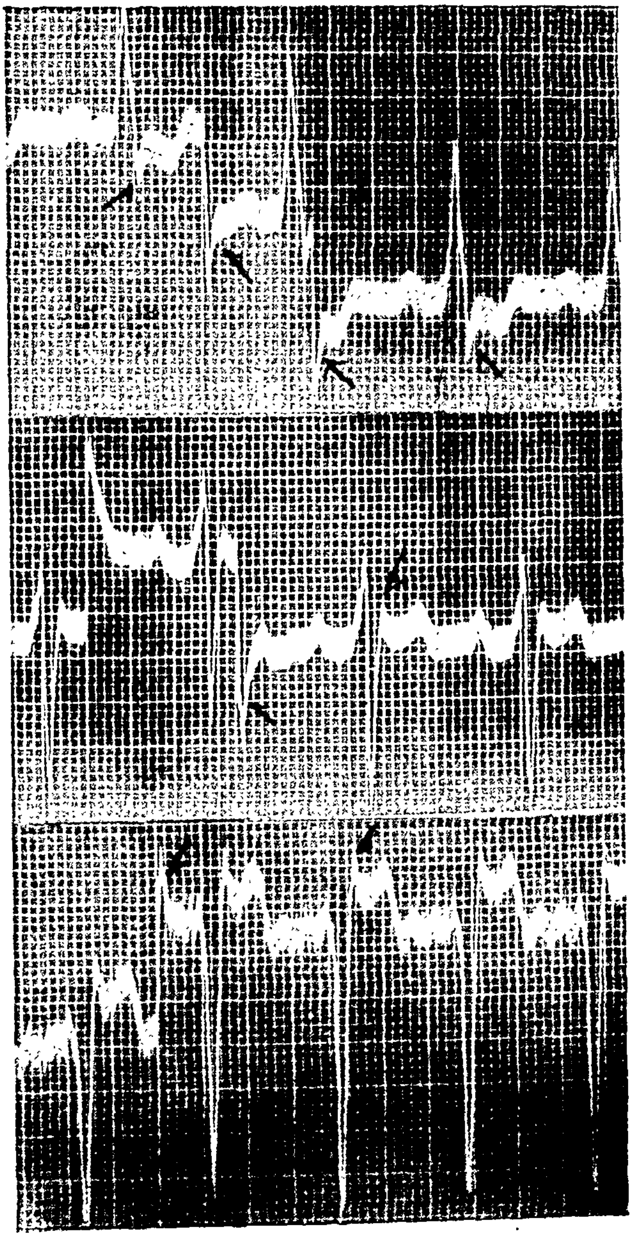

Fig. 4.—Record taken with the string galvanometer of a patient with very high resistance. Note the overshooting after the standardization jump, the large amplitude of QRS group and overshooting after the R-wave in Lead I and after the S-wave in Leads II and III.

This seems to be one of the obvious advantages of this type of instrument, and so it was with great surprise that I observed an article in the AMERICAN HEART JOURNAL, October, 1928,[1] in which it was claimed that overshooting is recorded by the amplifier tube instrument

—in fact that it is an integral part of all records by this instrument, so that for the purpose of examining the exact form of the electrocardiographic waves this instrument is useless.

It is an interesting fact that the record in Fig. 4 of the above article shows something which looks very much like the distortion due to overshooting in the last two complexes of the record. It seems to me that from the evidence presented by the author, his conclusion is quite unjustified; in fact, it seems that this conclusion is incorrect for reasons which will be presented. First, assuming that the overshooting in the records taken with the string galvanometer is due to capacitance,

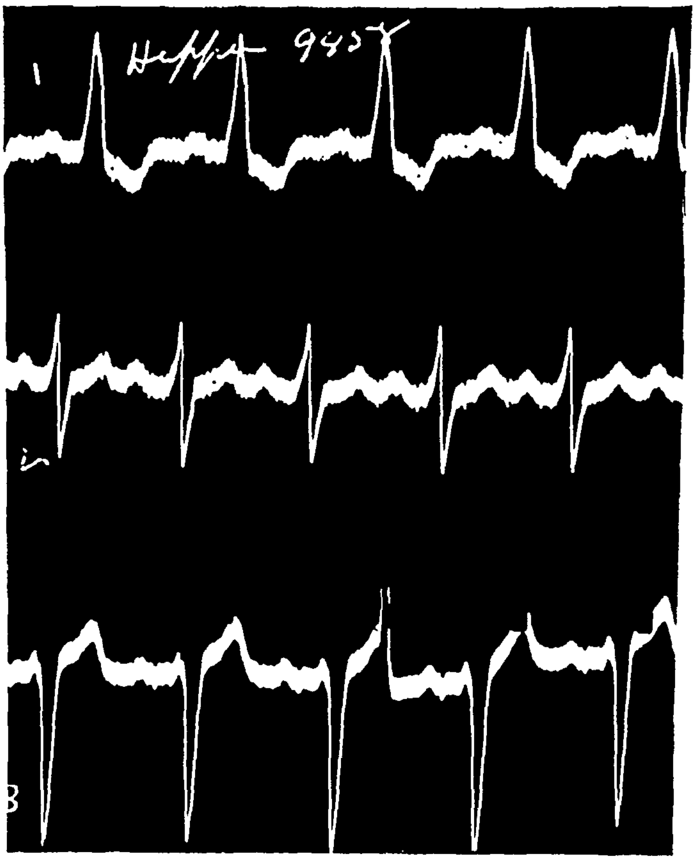

Fig. 5.—Record of the same patient with the amplifier tube instrument. Note the small size of the QRS group, and the absence of overshooting after the R- and S-waves.

there must be a flow of current to be impeded by the capacity resistance. In the string galvanometer there is a flow of current, but in the circuit of the patient and the amplifier tube there is no such flow of current,* the instrument being really a potentiometer. Since there is no flow of current, there can be no charging up of capacity; and therefore the overshooting which with the string galvanometer is due to the charging up of capacity, cannot occur. Second, a patient has

*There is a shunt of 900,000 ohms across the patient's circuit, but this resistance is so high that the flow of current is practically nil.

been found whose electrocardiogram shows a very sharp, almost right-angled turn from the R-wave into the beginning of the T-wave, as will be seen in Fig. 2, Lead I. The slightest overshooting would become apparent as the appearance of a small S-wave or at least some downward deflection following the R-wave. A record taken with the General Electric instrument is shown in Fig. 3, and it will be seen that not only are the waves of the same height and form in these two figures, but at this critical point the R-wave turns into the T-wave without the slightest evidence of overshooting; in fact, exactly as it does in the record taken with the string galvanometer.

Dr. Dock has compared these two types of instrument as if they depended upon the same electrical principles for their operation; this has given rise to the error into which he has fallen. The apparent overshooting in the standardization curve of the Victor instrument is easily explainable when one inquires into how this deflection is produced. The current which gives rise to this deflection is drawn from the same battery which charges the filaments of the amplifying tubes; this slight drain of current from the battery gives rise to a slight fall in the charge upon the filament, and accordingly a difference in potential between the filament and the grid of the tube is set up, which produces the movements of the indicator in question.* It would be impossible for a similar distortion of the electrocardiogram to occur while taking the patient's record, because the current which activates the galvanometer at that time is drawn from the patient and not from the battery which charges the filament. It is impossible to say what gave rise to the distortion of the current which was observed by Dr. Dock, but it seems impossible in view of the above that it could have the origin to which he ascribes it. The new instrument has certain advantages and disadvantages in comparison with the old; but since none of the disadvantages are vital to the obtaining of a correct record, it seems necessary to deny this erroneous statement which might throw the apparatus into unwarranted disuse.

REFERENCE

1. Dock, Wm.: The Distortion of the Electrocardiogram by Capacitance 4: 109, 1928.

*This, it will be seen, is an entirely different electrical process from that which gives rise to the overshooting with capacity resistance in the string galvanometer circuit.

THE TREATMENT OF ADAMS-STOKES SYNDROME DUE TO AURICULOVENTRICULAR BLOCK*

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The treatment of Adams-Stokes syndrome due to auriculoventricular block is in the vast majority of cases so unsatisfactory that any therapeutic measure which appears to afford a reasonable prospect of success is well worthy of a trial. The striking success following the administration of barium chloride in a case of very exceptional severity, in which other measures had completely failed, suggests that this drug should invariably be tried in this condition; and the satisfactory result following the exhibition of barium chloride by mouth together with adrenalin hydrochloride hypodermically in a case of moderate severity in which the administration of barium chloride alone was quite ineffective is also of considerable therapeutic importance.

We propose to deal with the subject in the following order: (1) Some general observations regarding the pathogenesis of Adams-Stokes syndrome. (2) The aim and the rationale appertaining to any therapeutic measure. (3) The rationale and the comparative value of various therapeutic measures, including barium chloride and adrenalin.

THE PATHOGENESIS OF ADAMS-STOKES SYNDROME

Adams-Stokes syndrome occurring in auriculoventricular block is due to temporary anemia of the brain, the result of bradycardia. The attacks may occur under one of the following conditions: (1) Suddenly developed, transient, complete auriculoventricular block. Several cases of this kind have been reported. The conduction of the stimulus for contraction along the auriculoventricular junctional tissues is normal except that there is a liability to transient interruptions. Lewis[1] is of opinion that such transient interruptions may occur in cases in which there is a lesion of the auriculoventricular junctional tissues. Cohn, Holmes and Lewis[2] have reported a case in which the fibers of the auriculoventricular bundle were found on post-mortem examination to be separated by large venous sinuses; the intermittent swelling of which, they considered, was responsible for the attacks. (2) Partial heart-block in which there occurs either an intermittent period of complete heart-block, resulting in a temporary standstill of the ventricles, or, rarely, merely a temporary increase in the grade of the partial heart-block, resulting in a temporary increase in the degree of the bradycardia. (3) Complete heart-block in which the con-

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dition has become *permanently* established, especially if the ventricular rate is below 30 per minute. In these cases pauses of unusual length, due to temporary standstill of the ventricles, the result of diminished irritability of the ventricles, may occur. Taking cases as a whole, Adams-Stokes syndrome is most commonly met with in patients with a severe grade of partial heart-block in whom complete block is developing. When complete heart-block has become permanently established, the ventricles apparently tend to become accustomed to the condition, and the pauses of unusual length referred to are not so likely to occur. One or more of the three following morbid affections may be responsible for the bradycardia which causes the Adams-Stokes syndrome in auriculoventricular block, namely: (1) a gross lesion of the auriculoventricular junctional tissues—sclerotic, less frequently gummatous, or, rarely, acute inflammatory; (2) overaction of the vagus; (3) diminished irritability of the ventricular myocardium.

THE AIM AND THE RATIONALE APPERTAINING TO ANY THERAPEUTIC MEASURE

The aim of any therapeutic measure is to increase the ventricular rate. Resolution of the auriculoventricular junctional lesion is only possible in cases of gummatous infiltration and acute inflammatory changes, and in the latter it is the usual sequel. In view of the facts that sclerotic changes account for the majority of cases in which there is a lesion of the auriculoventricular junctional tissues and that resolution of sclerotic changes is not possible, it naturally follows that attention should be directed to any other possible factor or factors which may be partly responsible for the bradycardia. In this connection, in partial heart-block, the indication is to counteract any possible vagal overactivity which may tend to increase the degree of existing block; while in both partial and complete heart-block the indication is to increase stimulus production, excitability and contractility of the heart muscle itself, with the object of preventing temporary ventricular standstill, or, if such should occur, of diminishing its duration.

THE RATIONALE AND THE COMPARATIVE VALUE OF VARIOUS THERAPEUTIC MEASURES

Antisyphilitic Measures.—A number of cases have been recorded in which appropriate and adequate antisyphilitic treatment appears to have been rewarded with recovery. These are cases in which the auriculoventricular block is the result of gummatous infiltration.

Potassium Iodide.—It may be worthy of note that when the cause is other than syphilis, potassium iodide, by its depressing effect on the ventricular muscle, may even aggravate the complaint, as in one of the cases reported by Herrmann and Ashman,[3] and in a case observed by Strauss and Meyer.[4]

Thyroid.—Because the administration of thyroid extract causes tachycardia in the normal heart, which they thought was probably due

either to stimulation of the sympathetic nerves or to direct stimulation of the sinus node, and also because in thyrotoxic hearts there is irritable and rapid cardiac action, with concomitant myocardial degeneration, Blackford and Willius[5] administered large doses of thyroxin, the active principle of the thyroid gland, to four patients who were subject to Adams-Stokes syndrome due to complete auriculoventricular block. In each case there was an increased ventricular rate, cessation of the attacks, and a marked improvement in nutrition. They attributed this to thyroxin directly increasing the idioventricular rate. Later, however, Aub and Stern[6] reported a case of complete heart-block without Adams-Stokes syndrome, in which the administration of large doses of thyroid had no influence on the ventricular rate, although the rate of the auricles was materially increased. Willius[7] after further investigation came to the conclusion that the beneficial effect of thyroid extract in patients subject to Adams-Stokes syndrome is not due, as he originally thought, to an increase in the idioventricular rate, but to what he described as an increased circulation rate and a consequent improved blood supply; the former being the result of increased metabolism causing an augmentation of the volume output of the blood for each beat and a relatively dilated arteriocapillary system. Drake[8] has recently reported a case of complete auriculoventricular block with Adams-Stokes syndrome in which the administration of thyroid extract at first caused a temporary resumption of normal rhythm; but a second trial of the drug resulted in alternating periods of 2:1 partial block and complete block. In this case, therefore, the drug does not appear to have been of any permanent value in reducing the frequency of the Adams-Stokes attacks, and its administration was ultimately stopped, because of nausea.

Atropine.—Since the action of atropine is to paralyze vagal activity, its employment is only likely to prove successful when Adams-Stokes syndrome depends upon overaction of the vagus. It has been demonstrated in man, by the employment of graphic methods, that stimulation of the vagus, by means of compression in the neck, by the act of swallowing, or by pressure upon the eyeball, may, by diminishing conductivity of the auriculoventricular junctional tissues, induce a transient heart-block, which is abolished by atropine. It has been shown further that stimulation of the vagus by these methods may, in the same way, induce a temporary increase in the degree of a preëxisting heart-block. The digitalis series of drugs also may, by their action on the vagus, produce a condition of heart-block, which is abolished by the administration of atropine. It should be noted, however, that persistent block of a severe grade is not vagal in the vast majority of cases, since it is unaffected even by full doses of atropine. This is confirmed by experimental work on dogs by several workers (Erlanger and Hirschfelder,[9] Fredericq,[10] Kahn,[11] van Egmond[12]). They showed

that in a heart in which the auriculoventricular bundle was destroyed, stimulation of the vagus no longer exercised any influence on the ventricles. They regard this as probably due to the fact that in some part of the course of the auriculoventricular tissues the pathway of the branches of the vagus nerve must have been broken. It is possible, therefore, that in Adams-Stokes syndrome due to partial heart-block, atropine may sometimes be of service by paralyzing vagal overactivity and so improving conductivity of the auriculoventricular junctional tissues. Hirschfelder has suggested that atropine may also improve the nutrition of the auriculoventricular tissues, by increasing the velocity of the circulation. In the case of Adams-Stokes syndrome due to complete heart-block, atropine is totally ineffective; indeed, it may even aggravate the complaint, as in a case of Cohn and Levine,[14] and in a case of Herrmann and Ashman,[3] in both of which the administration of the drug was followed by an increase in the rate of the auricles, without any corresponding increase of conductivity and of the ventricular rate, so that the relative degree of block was actually increased.

The Digitalis Series of Drugs.—When Adams-Stokes syndrome occurs in patients with partial heart-block, the administration of digitalis is contraindicated, since in these cases digitalis only increases the degree of the existing block. Heart-block produced by digitalis is usually due to stimulation of the vagus and is generally abolished by the exhibition of atropine. Cases do occur, however, in which atropine has no effect; in such cases the block must be attributed to a direct action of the drug on the auriculoventricular junctional tissues. When Adams-Stokes syndrome occurs in cases of complete heart-block, digitalis may be of value by increasing the excitability and contractility of the heart muscle, and so increasing the ventricular rate; indeed, Tabora[15] and Erlanger[16] found that in cases of experimentally produced complete heart-block digitalis caused a gradual increase in the ventricular rate to double its former level. The observations of these two workers were confirmed by van Egmond,[12] and by Rothberger and Winterberg,[17] who observed that digitalis increases the rate and force of the contractions of the ventricles, and in large doses may even induce paroxysms of premature contractions, which may terminate in ventricular fibrillation.

Caffein and Theobromin.—Van Egmond[12] found that in experimentally produced complete heart-block, the administration of caffein caused a transient increase in the rate and force of the ventricular contractions. It has also been found experimentally that diuretin, a compound of theobromin and sodium salicylate, has the effect of dilating the coronary arteries, thus improving the nutrition of the heart muscle. Notwithstanding these observations, Hirschfelder[13] is of opinion that caffein and theobromin are of no value in Adams-Stokes syndrome.

The Nitrites.—Strauss and Meyer[4] observed in a case of transient heart-block with Adams-Stokes attacks that nitroglycerin caused an increase in the pulse-rate for a short period. The drug, however, had no influence in preventing the recurrence of the attacks. These observers are of opinion that because of the vascular dilatation produced by nitroglycerin, there is an automatic increase in the pulse-rate in order to maintain an efficient circulation. In their case, nitroglycerin appeared to be more effective when the patient was under the influence of barium chloride. We cannot say that we have ever found the nitrites of any value.

Adrenalin.—Within recent years, a number of cases have been recorded in which the treatment of Adams-Stokes syndrome by adrenalin has been followed by gratifying results. The effect of the drug is usually to increase the rate of the heart, by stimulating the sympathetic nerve endings in the cardiac muscle. It also stimulates the vagal inhibitory center, and, if the vagal tone is good, this may result even in an actual slowing of the heart (Meek and Eyster,[18] Hoskins and Lovette,[19] and Korns and Christie[20]). Most observers (Cushny,[21] Hirschfelder[13]) are of the opinion that the drug also has the effect of dilating the coronary arteries, with resultant improvement of the nutrition of the myocardium. In a heart in which the auriculoventricular bundle has been destroyed, stimulation of the sympathetic—unlike stimulation of the vagus—has still a definite influence upon the rate of the ventricles (H. E. Hering[22]). The administration of adrenalin should, therefore, be followed by an increase in the ventricular rate. Such was noted by Cullis and Tribe,[23] who, working on cats and dogs, demonstrated that small doses of the drug caused an increase in the rate and force of the contractions of the auricles and ventricles, both before and after section of the auriculoventricular bundle. Other observers (van Egmond,[12] Routier,[24] Hardoy and Houssay,[25] and Clerc and Pezzi[26]) agree that the administration of adrenalin after the induction of experimental complete heart-block causes an acceleration of both the auricular and ventricular rates and also the occurrence of premature ventricular contractions. Kahn[27] found that when injected intravenously into dogs adrenalin produced heart-block. Routier,[24] on the other hand, actually noted a temporary disappearance of an experimentally produced heart-block after the exhibition of a moderate dose of adrenalin. He attributed this to the stimulation of the sympathetic nerve endings in the auriculoventricular bundle resulting in improved conductivity. This observation, however, has not been confirmed by any other experimental workers.

The *clinical* effect of adrenalin in cases of Adams-Stokes syndrome appears to have first been described in 1916 by Danielopolu and Danulescu,[28, 29] who employed it in a case of complete heart-block and also in a case of partial heart-block. In both cases there was an increase in the auricular and ventricular rates and also the occurrence of pre-

mature ventricular contractions. The partial heart-block was abolished, but the complete block was unaffected. Later, Strisower[30] reported a case of complete heart-block in which the injection of adrenalin, 0.5 c.c. of 1/1000 solution, was followed by an increased ventricular rate and a temporary return to the normal rhythm. A month later the patient exhibited 2:1 auriculoventricular block, which was abolished, but only for a few seconds, by a further exhibition of adrenalin. More recently, Parkinson and Bain[31] described a case showing varying degrees of partial heart-block, in which adrenalin facilitated conductivity when partial block was present but had no effect when the block was complete. Several other observers (Arrilaga,[32] Lutembacher[33]) have noted an increase in the auricular and ventricular rates, together with premature ventricular contractions, without, however, any alteration in the degree of block. Lutembacher[33] further noted that after an initial acceleration there was a slowing of the auricular and ventricular rates. Phear and Parkinson,[34] Feil,[35] and others, have reported cases in which the temporary standstill of the ventricles determining the attacks was abolished—without, however, any change either in the usual heart rate or in the degree of the existing block—with consequent abolition of the Adams-Stokes attacks. Korns and Christie,[20] on the other hand, described a case of 2:1 heart-block, in which treatment by adrenalin resulted in an increase in the degree of the block, although there was a coincident increase in the auricular and ventricular rates. They attributed the increase in the degree of the block to central vagus effects.

It is thus seen that both experimentally and clinically adrenalin may prevent a temporary standstill of the ventricle, by increasing the ventricular rate; it may improve conductivity and thus lessen the degree of any existing partial heart-block and exceptionally may even temporarily restore normal rhythm in complete heart-block; and it may produce premature contractions. It should be noted, however, that when vagal tone is good, the drug may occasionally, by its central vagal effect, increase the degree of existing block and may also increase the rate of the auricles out of proportion to the increase in the rate of the ventricles. Nevertheless, because of its action in the great majority of cases, it is indicated in cases of Adams-Stokes syndrome due to auriculoventricular block, especially during an actual attack.

The great disadvantage of adrenalin is that its action is of very short duration; therefore, the drug is not often effective when employed in the intervals between the attacks with the object of preventing their recurrence. When used for this purpose, it may be administered either subcutaneously or intramuscularly, in a dosage of from 5 to 10 minims of 1/1000 solution thrice daily. Adrenalin is, however, the only potent therapeutic measure at our disposal during an actual attack. It is necessary to point out that when—as in the vast majority

of cases—the attack is due to a temporary standstill of the ventricles, with consequent temporary cessation of the circulation, intracardiac injection is necessary, because the beneficial effect of the drug is due to its action in stimulating the sympathetic nerve endings in the heart muscle. The dose should be 0.5-1 c.c. of $1/1000$ solution. In the rare cases in which the attacks are due to merely a temporary increase in the grade of an existing partial heart-block, the drug may be effective even if given subcutaneously or intramuscularly.

Ephedrin.—Ephedrin has recently been employed as a substitute for adrenalin. It is the active principle isolated from the plant Ma Huang, which has been used as a medicine by the Chinese since antiquity. The chemical composition of ephedrin is closely allied to that of adrenalin, and the drug has a similar pharmacological action. It differs from adrenalin, however, in that its effect persists for several hours; and, moreover, it has the great advantage of being effective when administered orally. The first case in which ephedrin was employed in auriculoventricular block was one reported by Miller.[36] There was complete heart-block but no history of Adams-Stokes attacks. A moderate rise of blood pressure, an increase of both the auricular and ventricular rates—without, however, affecting the degree of the auriculoventricular block—and changes in the shape of the ventricular complexes followed the administration of the drug. Stecher[37] has recently reported favorably of the employment of ephedrin in a case of complete heart-block with Adams-Stokes syndrome. Although the exhibition of barium chloride resulted in some degree of improvement, the attacks still continued. Ephedrin was then administered, by mouth, in doses of 30 mgm. thrice daily for one week, followed by 20 mgm. thrice daily for two weeks. There was a complete absence of attacks during the administration of the drug, and afterward for a further ten weeks during which the patient was under observation. The highly successful result in this case would strongly suggest that further investigation of this drug is advisable.

Barium Chloride, and Barium Chloride Together With Adrenalin.—The value of barium chloride in the treatment of Adams-Stokes syndrome is due to the action which the drug has in increasing the irritability of the heart muscle. It has a characteristic action on many forms of muscular tissue, i.e., the contractions become stronger and very greatly prolonged. Junkemann[38] observed that the frog's heart at first beats more strongly and its rate is diminished; later it develops a rapid, irregular, idioventricular rhythm; and finally it stops in systole. Boehm[39] noted that in the case of mammals moderate doses of the drug cause an acceleration of the ventricular rate and an increase of blood pressure, but that large doses bring about a standstill of the left ventricle in systole. Ringer,[40] Brodie and Dixon,[41] Magnus,[42] and others agree with the findings of both these observers. It is be-

lieved that since its action is unaffected by curara, the drug acts directly upon the contractile substance of the muscle and not upon the nerve endings. Rothberger and Winterberg[43] carried out a series of detailed experiments on dogs concerning the action of barium chloride and calcium chloride, controlling their findings by means of the electrocardiograph. They found that both drugs increase the irritability of the cardiac muscle. After the administration of 5-10 mgm. of barium chloride intravenously, the heart could no longer be brought to a standstill by a simultaneous stimulation of the sympathetic and vagus nerves, which is the case in the normal heart. After 25-50 mgm. were administered, stimulation of the sympathetic, either directly or by means of adrenalin, caused the ventricular rate to be increased and also the occurrence of runs of ventricular premature contractions. With 50-100 mgm., the runs of premature contractions occurred spontaneously. They ceased in 5-10 minutes; but they could be readily evoked again, either by direct stimulation of the sympathetic, or by stimulation with small doses of adrenalin or nicotine. The diverse appearance of the electrocardiograms indicated that the ventricles had been stimulated at numerous points. With still larger doses of barium chloride, ventricular fibrillation ensued. Practically the same results are obtained when calcium chloride is employed, but larger doses of this drug are necessary. The contractility of the heart muscle is increased, and the blood pressure is raised 10-20 mm. of mercury by both drugs. The rate of the auricles is increased, but to a less extent than in the case of the ventricles. These workers are of opinion that barium chloride has no notable effect on the sino-auricular node, or on the auriculoventricular node. Van Egmond,[12] in cases of heart-block experimentally produced in dogs, confirmed the conclusions of Rothberger and Winterberg.[43] The importance of the foregoing observations lies in the fact that they show that barium, and, to a less degree calcium, increase the ventricular rate, either by stimulating the excitability of the existing idioventricular pacemaker, or by calling into action new ectopic ventricular foci. This may be produced by barium alone if used in a moderately large dosage; but stimulation of the sympathetic—which may be readily obtained by the administration of a small dosage of adrenalin—is also necessary if only a comparatively small dosage of the drug is used. In the treatment of Adams-Stokes syndrome, therefore, barium chloride alone, or barium chloride in combination with adrenalin, may be expected to be of definite therapeutic value.

The earliest clinical case of Adams-Stokes syndrome treated by barium chloride was reported by Wilson and Herrmann.[44] This was one of transient complete auriculoventricular block, thought possibly to be due to transient engorgement of large blood sinuses in the auriculoventricular node. At the suggestion of S. A. Levine,[14] the drug was

administered, in doses of ½ gr. ter in die, for a period of 38 days (May 18 to June 24), but without any effect in preventing the recurrence of the attacks. Shortly afterward, Cohn and Levine[44] reported the effect of the administration of barium chloride in three patients suffering from frequent Adams-Stokes syndrome. The usual therapeutic measures, including adrenalin, in each case failed to prevent the recurrence of the attacks, but barium chloride given orally proved successful. The following is a brief account of these cases.

CASE 1.—Male. Aged 55 years. A case of exceptional severity. The patient's condition had been steadily becoming worse until the administration of the drug was commenced. He was continually passing in and out of attacks of syncope, being conscious only about half the time, his condition resembling that of status epilepticus. The day following, although complete auriculoventricular block still persisted, there was an absence of long pauses and of attacks. Only 30 mgm. three times daily for two days were exhibited. The patient remained free from attacks for some weeks. After leaving the hospital, he began again to have frequent attacks. Calcium lactate, 1 gr. ter in die, was given, and the attacks ceased. Sudden death, however, occurred ten months after the commencement of barium chloride.

CASE 2.—Male. Aged 32 years. A case of moderate severity. Thirty mgm. of barium chloride four times daily for four days, after which 15 mgm. four times daily for three days, i.e., a total of 660 mgm., was exhibited. Together with the barium chloride, adrenalin, 0.3 c.c., was administered subcutaneously, four times daily for two days; after which it was reduced to 0.2 c.c. four times daily during the remainder of the time. After the commencement of the drugs, the patient had only one slight attack (on the seventh day), and more than a year after his discharge from hospital he was reported to have remained free from attacks and to be in excellent health.

CASE 3.—Female. Aged 52 years. A case of very considerable severity. Thirty mgm. of barium chloride ter in die was administered for nine days, i.e., a total of 810 mgm. This was followed by an interval of ten days, during which time the patient was discharged. The drug was then resumed, in the same dosage, for 10 days. The patient had remained free from attacks during this time. There was, however, a recurrence of the attacks, more severe than previously, ten days after cessation of the second course. The patient was readmitted to hospital and was kept alive by injections of adrenalin for about 20 days. At the end of this time barium chloride was resumed in doses of 30 mgm. four times daily for 44 days. It was then omitted for 36 days and during the whole of both these periods the patient remained free from attacks. She was then discharged from hospital, and the drug was continued for seven days, after which it was taken irregularly. The patient died suddenly seven months after the commencement of treatment by barium chloride and about three weeks after the discontinuance of regular doses of the drug.

Later, Levine[45] published a communication in which he stated that he had received information from two physicians to the effect that they had found that barium chloride was successful in preventing the recurrence of frequent Adams-Stokes attacks. A further case was reported by Levine and Matton,[46] in which, after the administration of adrenalin by the intracardiac method during Adams-Stokes attack,

barium chloride, in doses of 30 mgm. four times daily for seven days, was given, with the object of preventing the recurrence of the attacks. The patient died two months after the cessation of the drug. Herrmann and Ashman[3] have described two cases of Adams-Stokes syndrome treated with barium chloride, one of a severe grade of partial heart-block and the other of complete block. Barium chloride was exhibited in large dosage, without any toxic effect. One patient received a total of 10.98 gm. in 67 days, after which the dosage was reduced to 50 mgm. daily. The other patient received 840 mgm. in 8½ days. In both cases there was a remarkable improvement, the pulse-rate in one increasing from 26-34 to 72, and in the other case from 34-38 to 50-70. In the second case, however, the administration of antispecific treatment (mercury and iodide) should be taken into account. Herrmann and Ashman[3] are of opinion that in their cases barium chloride certainly increased the irritability of the idioventricular pacemaker. They are further of the opinion that, in order to maintain a minimum concentration of the drug, it should be taken continuously in small doses; indeed, they believe that its intermittent use may even be dangerous.

Heard, Marshall and Adams[47] have published a case of Adams-Stokes syndrome in a patient showing varying degrees of partial heart-block—a mere increase in the P-R interval, 2:1, and 3:1 alternating. A total quantity of 5 gm. of barium chloride was administered during a period of three months. The result was not only not beneficial, but also the attacks continued with gradually increasing frequency. B. T. Parsons-Smith[48] has reported a case of complete auriculoventricular block, with a ventricular rate of 30 per minute, subject to Adams-Stokes syndrome. The exhibition of adrenalin at first prevented the occurrence of the attacks. Later, owing to their recurrence, barium chloride, ½ gr. doses twice daily, was given. A gradual increase of the ventricular rate was noted, until at the end of four months an electrocardiogram showed normal rhythm, with a rate of 72. Still later, however, in spite of the continued administration of the drug, reversion to complete heart-block occurred, but without Adams-Stokes attacks, and there was also an improvement in the exercise tolerance. Strauss and Meyer[4] have recently published a case of transient complete heart-block with Adams-Stokes syndrome, in which the employment of a daily dosage of 120 mgm. of barium chloride was followed by an almost entire cessation of the attacks and, although the dosage was relatively large, without any toxic symptoms. It is interesting to note that whereas the majority of cases of transient complete heart-block (Carter and Dieuaide[49]) pass into permanent complete heart-block, it did not occur in this case. Strauss and Meyer[4] further noted that, while pressure on the vagi produced complete heart-block before the administration of the drug, this did not occur during its administration.

We will now describe two cases which were admitted to the National Hospital for Diseases of the Heart, London, England, under the care of one of us (F. W. P.).

CASE REPORTS

CASE 1.—Mr. M., admitted to hospital, July 23, 1926. The following history was obtained: Age, 69 years; widower; married twice; had seven children; five living; two died in infancy. A clerk. Smokes 6-7 oz. tobacco per week. A teetotaller. Ten years ago he had "rheumatism," in the joints of arms and legs, disabling him, lasting about a year. No history of specific disease. About ten years ago, in his usual health, on a very hot day while walking in the sun, having had no premonitory symptoms, he suddenly fell to the ground unconscious, the loss of consciousness lasting only a few seconds. Did not bite tongue, nor pass urine or feces. After recovering consciousness, he continued his work. Many weeks later, a second similar attack, and recurrence of such about once a month for six years, then free for three years. About a year before admission to hospital, attacks began again. For first two or three weeks, two or three attacks per diem, occurring at intervals varying from five minutes to some hours. The attacks gradually increased in frequency, until they reached forty or more per diem, and sometimes patient was continually passing in and out of attacks. Has been in bed for four or five months. No diminution of frequency of attacks while in bed. Patient said that he occasionally felt the heart "stop," this immediately followed by feeling that he "is going." Patient's son-in-law, a qualified masseur, stated as follows: "At the commencement of attacks there is a definite, but transient, flush, followed by pallor of the cheeks, and cyanosis of the lips and nose. Period of loss of consciousness lasts up to four minutes." He sometimes thought the patient was dead. "There are sometimes convulsions, depending upon the length of time of unconsciousness. They affect the face, less frequently the arms, and still less frequently the whole body. They are sometimes accompanied by deviation of the eyes and of the mouth to either side. Stertorous breathing during severe attacks. No vomiting. Pulse rate between the attacks is 20-30 per min. At the commencement of attack, it falls to as low as 11 per minute, this invariably followed by a long pause, varying from 30 seconds up to three minutes. Pulse is very often palpable before return of consciousness, but sometimes both coincide." On one day about June 15 for about 12 hours, patient was continually passing in and out of attacks. Patient thought that he had sometimes been able to prevent an attack from coming on by taking an unusually long breath. Excepting during the three years that he was free from attacks, he suffered from shortness of breath on exertion. On admission: Pulse regular, unless, as was sometimes the case, extrasystoles were present, the latter sometimes occurring at irregular intervals and at other times after each ventricular beat. On admission the ventricular rate was 26 per minute; afterward it varied from 20-26 per minute, excepting when extrasystoles were present. No evidence of thickening of wall of radial artery, but that of brachial considerably so and rather tortuous. Blood pressure about 160-65 mm. Apex beat in the fifth intercostal space, and its force moderately increased. A rough, harsh systolic murmur over the whole precordium and the vessels of the neck. Physical signs of a moderate degree of emphysema. No nocturnal polyuria. Urine had S.G. of 1.014, contained a faint trace of albumin, but no sugar was present. On screening, left border of heart in nipple line, right border 2 inches to the right of the sternum, and transverse measurement of organ 6¾ inches—thus, considering age and build, much enlarged. The aortic shadow was diminished in translucency; its transverse measurement was increased, being 3¼ inches, and left margin was

curved. An electrocardiogram taken July 27 indicated marked left-sided preponderance and complete auriculoventricular block, and there was inversion of the T-wave in all leads, very slight splintering of the R-deflections, and an extrasystole, arising in the apical or left portion of the ventricle, after each ventricular complex of normal form in the second and third leads. Wassermann reaction negative. Subsequent progress: August 7, numerous attacks daily since admission. Pulse rate was counted during one of them. There was an absence of pulse for 10-15 seconds, and after an attack the rate was 12 per minute. August 12, numerous attacks daily still continued; 10 minims of 1/1000 solution adrenalin hydrochloride hypodermically during an attack, with no apparent effect. August 13, very numerous attacks, there sometimes being only three or four ventricular contractions between two attacks. During an attack the patient became pale, then after from five to ten seconds (timed) head dropped back, face became cyanosed, eyes deviated to the right, and clonic spasms of facial muscles commenced. Spasms extended to muscles of neck, and in the longer syncopal attacks they became general. With onset of clonic spasms, breathing became stertorous. During some attacks no ventricular contractions for 35 seconds. With the first ventricular contraction consciousness was rapidly regained and face became flushed. One attack lasted five minutes. On one occasion the resident medical officer pronounced patient to be dead and screens were placed round the bed. After attacks had been occurring every few minutes, 15 minims 1/1000 solution adrenalin hypodermically. This was followed immediately by an attack, but patient was free for about an hour afterward. Ventricular rate was 12 a half hour after injection. August 14, numerous attacks during the night and until 9:45 A.M., when 15 minims 1/1000 solution adrenalin were administered. At 12:15 P.M. had had only two subsequent attacks. An unusually long attack at 4 P.M. August 19, numerous attacks, including one long one, 15 minims 1/1000 solution adrenalin together with 1/100 gr. atropine given, with no effect, frequent vomiting. August 20, numerous attacks, including two long ones. One lasted 1 minute and 10 seconds, during which respiration ceased. Strychnine 1/30 gr., at 10:15 A.M., and 15 minims adrenalin at 3:30 P.M. Frequent vomiting. August 22, only four or five attacks, including one or two slight ones. August 25, attacks greatly reduced in number since August 20 until early that morning, since then fairly frequent but short attacks, fifteen minims 1/1000 solution adrenalin. August 26, 15 minims 1/1000 solution adrenalin hypodermically. August 27, 15 minims 1/1000 solution adrenalin hypodermically. September 8, electrocardiogram as before, excepting that extrasystoles in all leads. September 10, patient was continuing to have attacks, but of short duration. September 13, commenced liq. atropine, by the mouth, 1 min. thrice daily. September 24, no attacks for two days until that morning, then numerous minor attacks. September 26, was free from attacks for three days until this day; those of short duration returned. Ventricular rate 20. Jugular pulsations about 80. October 4, still having rather bad attacks. Pulsus bigeminus, ventricular rate being 40 and pulse rate 20 per minute. October 7, atropine suspended; barium chloride, ½ gr., twice daily, commenced. October 8, barium chloride, ½ gr., thrice daily. October 11, no attacks since commencement of barium chloride. October 15, three severe attacks. Ventricular rate 26, excepting when occasional coupling of beats. Barium chloride increased to gr. 1 thrice daily. October 25, no further attacks. Still on barium chloride, gr. 1, thrice daily. Ventricular rate 26, excepting when occasional coupling of beats. October 29, administration of barium chloride stopped. November 2, commenced to get up. November 4, free from attacks. November 5, electrocardiogram as before, but no extrasystoles present. Discharged from hospital November 11. March 4, 1929, patient had been free from attacks since

discharge from hospital, and led a fairly normal life. Ventricular rate 31. Blood pressure 216/74 mm. Electrocardiogram as on last occasion.

It will be noted that this was a case of Adams-Stokes syndrome of very exceptional severity occurring in auriculoventricular block in which complete success followed the administration of barium chloride after other measures had failed. As far as our knowledge of the literature on the subject goes, the case is a unique one.

CASE 2.—Mrs. M., admitted to hospital February 22, 1928. The following history was obtained: Age 65 years. Seven children, alive and well. Patient had influenza and was confined to bed for over a week in 1923; and was again confined to bed for about a fortnight in September, 1926. No other previous illnesses. Wind and strength up to normal until after second attack of influenza, since then increasing shortness of breath, palpitation and exhaustion on exertion. In the summer of 1927, while in a cinema, suddenly seized with "giddiness," immediately followed by loss of vision, i.e., "things went black," and a sensation of "heat" from the lower part of the back to the top of the head, immediately followed by momentary loss of consciousness, which patient described as "losing herself." Three or four more attacks, less severe, later in the day. Since then patient had been subject to attacks, consisting of the same symptoms. They lasted only for a few seconds, and were followed by a sense of exhaustion. She had never fallen during an attack but supported herself by laying hold of the nearest object. The attacks came on without apparent cause. Since the first attack patient had also been subject to giddiness, not followed by other symptoms. Just before December, medical attendant remarked to her that she had a "remarkably slow pulse." The attacks increased in frequency; and for some hours on one day during the first week in December they were so frequent as to be separated by intervals of only a few moments' duration, on account of which patient stayed in bed for a fortnight, at the end of which time they had diminished to two or three per diem. A recurrence of frequent attacks on January 1, 1928. On February 16, patient came in a motor car to the out-patient department of the hospital. While in the waiting room, she had at least seven attacks. She was admitted as an in-patient on February 22. On admission: Pulse was regular. Ventricular rate 36 per minute. No evidence of thickening of walls of radial or brachial arteries. Blood pressure 240/84 mm. Force of apex beat rather considerably increased. A rather loud systolic murmur and second sound rather considerably accentuated in the aortic area. A moderate systolic murmur at the apex propagated from the aortic area, becoming louder on lying down. No nocturnal polyuria, and nil abnormal on examination of urine. On screening, left border of heart ¼ inch outside midclavicular line, right border 1 inch to the right of the sternum, and transverse measurement 5¾ inches—thus, considering age and build, moderately enlarged. The aortic shadow is rather wide, measuring 2¼ inches. An electrocardiogram shows left-sided preponderance, inversion of T in Leads II and III, and complete auriculoventricular block. Wassermann reaction negative. Subsequent progress: At first 20-25 attacks per diem, but by February 28 they had diminished in frequency. On March 5, barium chloride, in pill form, ½ gr. twice daily, administered for seven days; then dosage was increased to 1 gr. thrice daily. No diminution in frequency of attacks. March 17, 1/100 gr. atropine hypodermically, with no effect. March 20, attacks as before. Ventricular rate 40 per minute. An electrocardiogram as before. April 14, atropine, 1/50 gr., hypodermically. Ventricular rate 36 per minute at time of injection, 36 fifteen minutes later, and 34 fifteen minutes later. April 20, attacks

continued without change. April 27, electrocardiogram as before. April 28, no diminution in frequency or severity of attacks. Was still on barium chloride, 1 gr., thrice daily. Commenced 5 minims 1/1000 solution adrenalin hypodermically thrice daily, which injections were continued. No attack since first injection of adrenalin. May 8, was very much better. No further attacks. Blood pressure 250/100 mm. Size of heart the same. May 11, electrocardiogram showed 2:1 auriculoventricular block instead of complete heart-block. May 21, patient up for half an hour; increased on May 23 to one hour. May 26, patient was still on barium chloride, in same dosage. Adrenalin hypodermically reduced to twice daily. May 29, felt much better. Still no further attacks. Ventricular rate 40 per minute. Blood pressure 230/90 mm. Barium chloride by the mouth and adrenalin hypodermically, both in same dosage, were continued. June 2, adrenalin hypodermically reduced to once daily. June 5, recurrence of attacks. Adrenalin hypodermically increased to twice daily. June 21, no recurrence of attack. Dosage of adrenalin hypodermically changed to 10 minims once daily. Patient was discharged June 26, still having 1 gr. of barium chloride thrice daily by the mouth, and 10 minims of adrenalin hypodermically once daily. January 28, 1929, the treatment by barium chloride by the mouth and adrenalin hypodermically was continued, but some time during Christmas week the daily dose of adrenalin was reduced from 10 to 8 minims. Patient's medical attendant recently taught her to give the hypodermic herself. She usually did this about midday, failing which, she postponed it until bedtime, in which event she did not feel nearly so well. She felt better than she had for two years. On examination: Pulse regular. Ventricular rate 48 per minute. Blood pressure 278/92 mm. On screening, heart as before. An electrocardiogram revealed 2:1 auriculoventricular block instead of complete auriculoventricular block.

It will be observed that this was a case of Adams-Stokes syndrome due to complete auriculoventricular block in which a satisfactory result followed the administration of barium chloride by mouth together with adrenalin hypodermically, and in which the use of barium chloride alone was quite ineffective. It is worthy of note that an electrocardiogram taken ten days after the commencement of the administration of adrenalin hypodermically, in addition to barium chloride by mouth, revealed 2:1 auriculoventricular block, instead of complete auriculoventricular block. An electrocardiogram taken on January 28, 1929, showed that the former was still present.

It would appear, therefore, from a study of the foregoing cases, that the exhibition of barium chloride, administered by the mouth, failing which, barium chloride together with adrenalin, the latter given either hypodermically or intramuscularly, is indicated for the prevention of the recurrence of Adams-Stokes syndrome due to auriculoventricular block. We would recommend the following: That barium chloride be administered, at first in doses of ½ gr. thrice daily. This dosage should, if necessary, be cautiously increased—stopping short of toxic symptoms—to 1 gr. thrice daily. With regard to adrenalin, 0.5 c.c. to 1 c.c. of $\frac{1}{1000}$ solution thrice daily until after the attacks have ceased for some time. The dosage of adrenalin should then be gradually diminished until the drug is omitted altogether. Still later, the dosage

of barium should be gradually reduced to the minimal dose found necessary to prevent the recurrence of the attacks.

SUMMARY

A. The pathogenesis of Adams-Stokes syndrome due to auriculoventricular block is described.

B. The primary aim and the rationale appertaining to any therapeutic measure is discussed. These are shown to be an increase in the ventricular rate, brought about in one or more of the following ways: (1) the resolution of the lesion, as, for example, in gummatous infiltration and acute inflammatory changes; (2) the counteraction of any possible vagal overactivity; (3) the increase directly of stimulus production, of excitability and of contractility of the heart muscle.

C. The rationale and the comparative value of various therapeutic measures are discussed.

Antisyphilitic treatment is indicated in Adams-Stokes syndrome due to auriculoventricular block when this is the result of gummatous infiltration.

Potassium iodide may even aggravate the complaint when the cause is other than syphilis.

Thyroid appears to be sometimes of value and may even be completely effective.

Atropine, administered between the attacks, in order to prevent their recurrence, is indicated in cases of partial heart-block in which there is vagal overactivity.

Digitalis is contraindicated in partial heart-block. It may be of value in complete heart-block.

Caffeine and theobromine are of no clinical value.

Of reported cases, the nitrites were found to be only of doubtful value in one case.

Adrenalin is of value in the great majority of cases. It is not often effective in preventing the recurrence of the attacks. When employed for this purpose, it may be administered either subcutaneously or intramuscularly. It is, however, the only potent therapeutic measure during an attack. When employed for this purpose, intracardiac injection is necessary, except in the rare cases in which the attacks are due to a merely temporary increase in the grade of an existing partial heart-block, in which event it may be given either hypodermically or intramuscularly.

Further investigation of ephedrin, administered by mouth, is advisable.

Barium chloride, given by mouth, should invariably be tried for the prevention of the recurrence of the attacks in cases of Adams-Stokes syndrome due to auriculoventricular block. If ineffective alone, the drug should be employed with adrenalin, the latter administered either hypodermically or intramuscularly.

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CONGENITAL HEART DISEASE; EXTREME CONGENITAL PULMONARY STENOSIS (TETRALOGY OF FALLOT); COLLATERAL PULMONARY CIRCULATION; MASSIVE RIGHT-SIDED VEGETATIVE ENDOCARDITIS*

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THE comparative rarity of congenital cardiac defects and the need for their further detailed clinico-pathological study seems to justify the reporting of all instructive cases. The type here presented, often called the "tetralogy of Fallot," is that which is met with most frequently by the practitioner. It is characterized by four anatomical changes, namely, (1) pulmonary stenosis, (2) defect in the interventricular septum, (3) dextraposition of the aorta, and (4) hypertrophy of the right ventricle. Characteristically, cyanosis, clubbing and polycythemia are present in varying degrees according to the extent of the irregularities in the circulation which interferes with oxygenation of the blood.

Clinically, the condition is important, not only because of its frequency, but also because, of the more serious cardiac anomalies, it permits a relatively long duration of life; and although the prognosis is always more or less grave, according to the extent of the lesion, something may be accomplished in treatment by regulation of mode of life and other measures. White and Sprague[1] have recently reported the interesting case of Gilbert, a noted American musician and composer who attained the age of 59 years, having suffered all his life from a marked degree of this type of disease. Great care to avoid fatigue and to guard against infection doubtless contributed much to prolong his life.

HISTORICAL

Sandifort in 1777 first described the condition which later became known as the tetralogy of Fallot. As long ago as 1814, Farre stated that it was the commonest malformation of the heart. The first extensive study, however, seems to be that of Peacock[2] who in 1866 was able to collect 60 published references to this anomaly. Fallot[3] in 1888 brought together clinical and pathological findings in a very clear manner, and since that time his name has been associated with this particular type of anomaly. In the more recent literature Dr. Maud Abbott's classical monograph[4] in the 1927 edition of Osler's Modern Medicine

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reviews completely our present knowledge of congenital heart disease. Her work is based upon the study of 850 defects with autopsy findings. A localized defect at the base of the interventricular septum occurred in 240 cases. Of these, 54 were classified as the primary lesion and 186 complicated other anomalies. Of these 186 cases of defect at the base, 95 were in cases of pulmonary stenosis or atresia, among which dextraposition of the aorta occurs 62 times. In Abbott's series the occurrence in the same heart of a defect at the base of the interventricular septum, pulmonary stenosis or hypoplasia of the developmental type, and dextraposition of the aorta makes up the commonest of all combinations in congenital heart disease. Hypertrophy of the right ventricle is always present and so constitutes the fourth pathological element in the complex.

PATHOGENESIS

Many earlier writers sought to explain the causal connection suggested by the association of these anomalies. The theories of their etiology and pathogenesis are too involved for discussion here, but a few points may be mentioned, however. All cardiac anomalies occur either as the result of arrest of growth at an early stage, or by fetal disease in the more fully developed heart. There is much evidence to point to the former as the etiological factor in most cases, including the condition described here. Those resulting from endocarditis in later fetal life are thought to be confined to a small group in which the stenosis is strictly limited to the valves, and with no associated septal defect. In cases of developmental origin the arrest must have occurred some time before the end of the second month of gestation at which time the heart is complete.

The explanation by Keith,[5] brought out over twenty years ago, is now generally accepted. He concluded that in the majority of the cases the stenosis is primary in the conus and is the result of an arrest of development at a stage when there existed in the heart a fourth primitive chamber, the bulbus cordis. Tracing the evolutionary changes from the fish and reptiles, Keith described how in the mammalian heart the bulbus cordis has become separated from the left ventricle and aorta and is completely incorporated in the right ventricle as the infundibulum of that chamber. This occurs during the first month of gestation. As he says, "The submergence of the bulbus constitutes a critical phase in the developmental metamorphosis of the heart, and it is during this time that malformations are apt to occur," so that whatever agent may be at work in producing these malformations must exert its effect at this early stage of development.

Fallot's tetralogy centers around the pulmonary stenosis which is the essential part of the anomaly, etiologically and clinically. Cyanosis is such a constant feature that morbus caeruleus and pulmonary stenosis

have been considered almost synonymous terms. The presence of an interventricular septal defect indicates that early stage at which the stenosis took place. The clinical aspects vary somewhat with the situation and extent of the deformity. These may profitably be considered in connection with the present case, which exhibited all typical symptoms and signs.

CASE REPORT

E. M., a female, aged 16 years, was admitted to the University of Michigan Hospital, December 10, 1928, complaining of "heart trouble."

Present Illness.—Cyanosis had been present since birth. As a child the patient was always backward. She did not walk until 3 years of age. At the age of 6, following whooping cough, the cyanosis became very prominent. She had always complained of cough and pain in the precordium on exertion. Cyanosis was much accentuated with increased muscular activity. Even after walking a block or so she was compelled to stop and rest. In spite of this the patient had always been

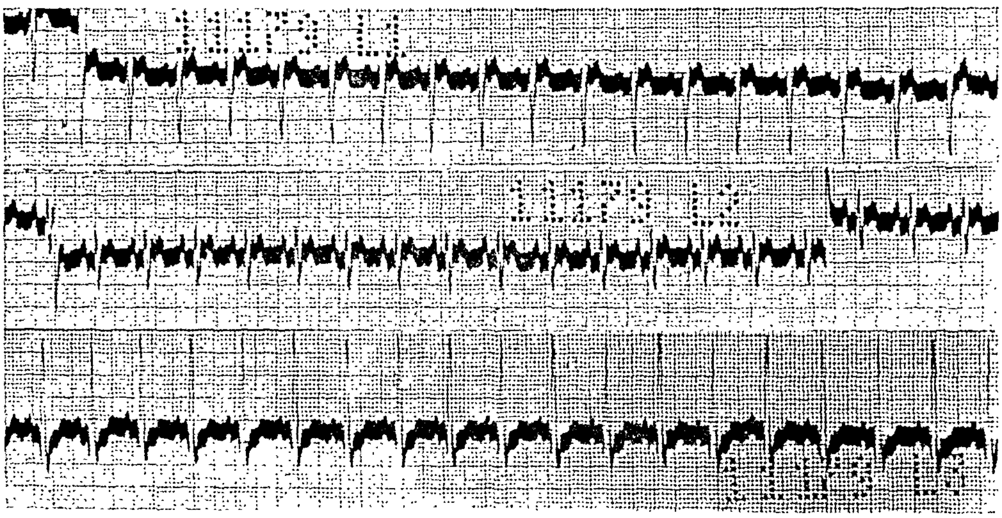

Fig. 1.—Electrocardiograph tracing showing marked right ventricular preponderance.

up and about. In the summer prior to admission she had used roller skates, but these were finally discarded because she had swelling of the ankles. About a month before entrance to hospital she had three teeth pulled. The gums continued to bleed. After two days she had a temperature of 102° F. A week later the temperature was still elevated, and the patient was confined to her bed. During the two weeks preceding entrance, gross blood was noted in the urine. She developed severe epigastric and precordial pain. She was tender all over the body and was troubled with an occasional dry cough. Shortness of breath was not prominent, but there was a deepening of the cyanosis.

Past History.—The patient was the last child of a family of eight; there were three sisters and four brothers living and well. Her mother was about 47 and her father 56 when she was born. The patient had smallpox, measles and whooping cough and had also been subject to occasional sore throats. She had always been constipated. She had grown to normal height but was always thin. Menses began at the age of 14 years and had always been irregular. The patient had been considered to some degree mentally deficient.

Family History.—Father died of heart disease at the age of 69. Mother died of Bright's disease at 60. As far as could be ascertained there was no history

of congenital heart disease in the family and none of her brothers and sisters had obvious abnormalities.

Physical Examination.—The patient was a poorly nourished, adolescent female, lying flat in bed with moderate dyspnea and marked cyanosis. The nose, lips, malar prominences and hands appeared purple. The gums were bleeding. The tongue gave the impression of dehydration. The tonsils were enlarged. The chest showed a bulging over the precordium. The sternocostal junctions were prominent. There was a marked scoliosis to the left in the dorsal region. A pulsation was noted in the third and fourth interspaces on the left. There was a questionable precordial thrill. The heart was enlarged to percussion, the borders being 11 cm. to the left in the fourth interspace, and 6 cm. to the right. The rhythm was regular, the rate 120. A loud systolic murmur was best heard in the

Fig. 2.—X-ray plate of chest showing large heart, cervical ribs and thoracic scoliosis.

second, third and fourth interspaces just to the left of the sternum. No diastolic murmur could be detected. The pulmonary second sound was moderately loud. The lungs showed only diminished breath sounds and a few râles at the left base. The liver was palpable just below the costal border. Edema was absent, but there was marked clubbing of the fingers and toes.

Laboratory Findings.—The Kahn test was negative. Urine showed a specific gravity of 1.020, with albumin and many granular and hyaline casts. Gross blood was present on one occasion. Blood examination showed: hemoglobin 100 per cent; red blood cells, 7,450,000, and the white blood count 19,500; *differential count,* polymorphonuclears 68, lymphocytes 31, eosinophiles 1. The blood culture was negative. Electrocardiograph tracings showed marked right ventricular preponder-

ance and sinus tachycardia (see Fig. 1). X-ray examination of the chest showed cardiac enlargement, scoliosis to the left, and bilateral cervical rib (see Fig. 2).

Course in Hospital.—At entrance the temperature was 103° F. and was continually above 100° and went as high as 105°. The pulse was rapid and the respirations at times were Cheyne-Stokes in type. The cyanosis decreased somewhat with absolute rest, but the weakness increased and the mental state became clouded. Oxygen was given but with no marked results. On December 17, 1928, a week after admission, the patient died.

Clinical Diagnosis.—Congenital heart disease, probably pulmonary stenosis with interventricular septal defect and a superimposed infection in the form of septicemia or bacterial endocarditis. Scoliosis. Bilateral cervical rib.

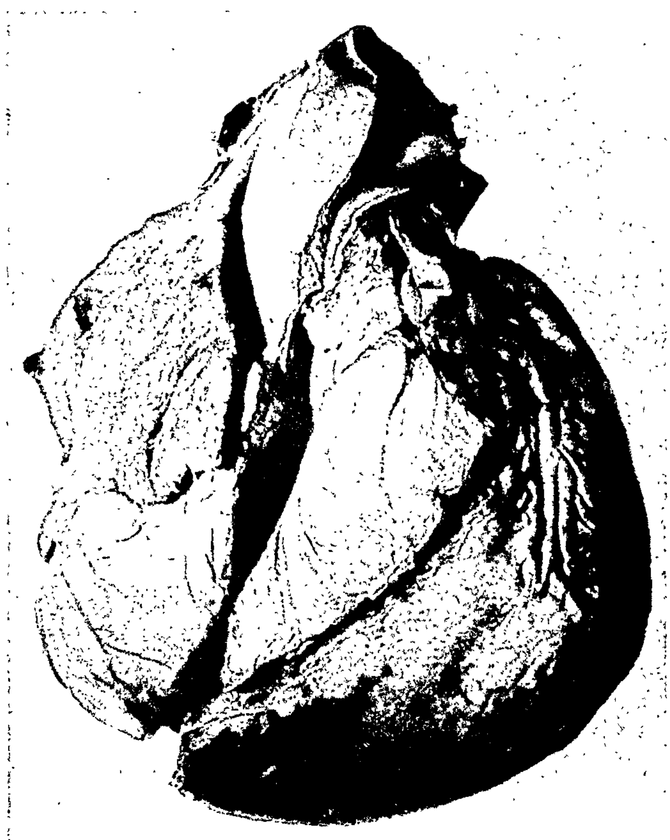

Fig. 3.—Anterior view of heart.

AUTOPSY

The summary of significant gross findings, apart from the heart, is as follows: Body was that of a poorly nourished, adolescent female, 154 cm. in length, showing the features of the asthenic type and having the appearance of an inferior degenerative constitution. There was a distinct brachygnathia. There was a marked thoracic scoliosis. There was very marked clubbing of all fingers and toes and a marked generalized cyanosis of the skin, with also a faint icteroid tinge. The spinal cord showed congestion and edema. There was an asymmetry of the calvarium with a depressed area measuring 6 cm. in diameter in the part of the cranium occupied by the posterior fontanel in the infant. This was evidently a congenital defect. The fifth and sixth costal interspaces were widened at their union with the sternum. There were bilateral cervical ribs. The one on

the right articulated at its tip with the first rib. The left had a free tip. The twelfth rib on either side was very short and rudimentary. The cardiac apex was in the fourth intercostal space halfway between the midclavicular and anterior axillary lines. The right border measured 6 cm. to the right of the midsternal line. The pericardium was apparently normal. (The heart will be described in detail below.) The lungs felt leathery. They were a dark purplish color from the extreme congestion but showed no evidence of pneumonia or tuberculosis. There were no pleural adhesions. The spleen was large, weighing 390 grams; the liver 1770 grams. Both showed evidences of chronic passive congestion. The kidneys were congested and showed swelling and a few small fresh anemic infarctions.

Microscopic examination showed a marked congestion of all tissues. The liver and spleen showed chronic passive congestion. In the lungs there was extreme congestion and edema, on a chronic passive congestion, and fibrosis. The renal glomeruli were usually large. One of the clubbed toes was examined microscopically and showed chronic productive periosteitis toward the tip with thickening of the blood vessels.

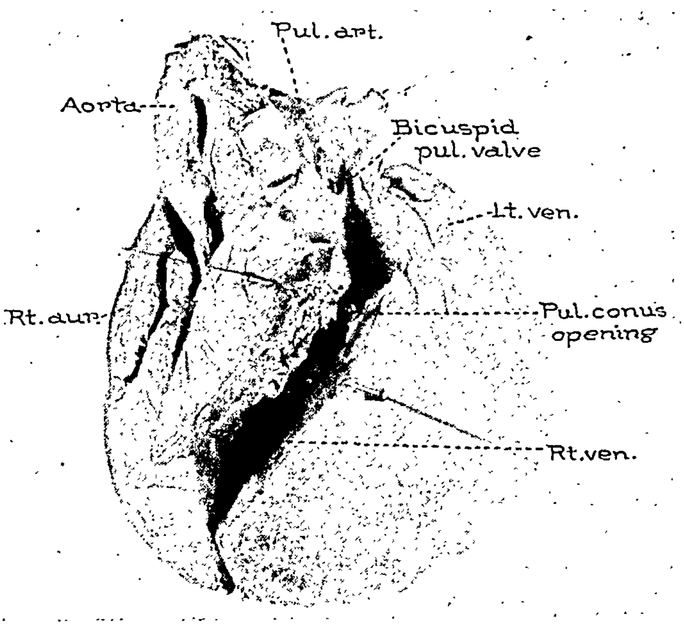

Fig. 4.—Anterior view of heart with pulmonary tract spread open.

DETAILED DESCRIPTION OF HEART

The heart weighed 290 grams. It is of a peculiar shape, being broad transversely in comparison with longitudinal measurements. The apex is broad and flat, lacking the conical shape as seen in the normal heart. Externally there is no division visible between right and left ventricles (see Fig. 3). The great vessels arise in the normal relationship, except that the aorta appears to arise from both ventricles, while the pulmonary artery is very small, thin walled, and arises anteriorly and to the left of the aorta. The transverse measurement across the ventricles at the widest point is 11 cm. The length from the base of the aorta to the apex is 9 cm., and from the superior vena caval opening in the right auricle to the apex 10 cm. The anteroposterior thickness of the ventricles is 6 cm.

The epicardium is smooth and shining. There is a moderate amount of subepicardial fat. The superior and inferior venae cavae appear normal in size and open into the right auricle in normal relationship. This cavity is moderately dilated. The muscular wall is slightly thicker than normal. The musculi pectinati

are prominent. One of these is attached only at its extremities and stretches across the opening of the superior vena cava a distance of 2 cm. Attached to this round muscular band, which is 2 mm. in thickness, there are several thread-like structures traversing the cavity with thin attachments on the superior wall of the auricle (Chiari's network).

The valve of the inferior vena cava persists but is not prominent. The fossa ovalis is in the normal position. From its superior aspect an elliptical interauricular opening persists. This patent foramen ovale, valvular in form, will admit a probe 1 cm. in diameter. The coronary sinus, protected by its valve, opens in its normal relationship just below the limbus of the fossa ovalis.

The pars membranacea septi as viewed from the right auricle, is seen to lie in its normal position "at the base of the medial cusp of the tricuspid valve just

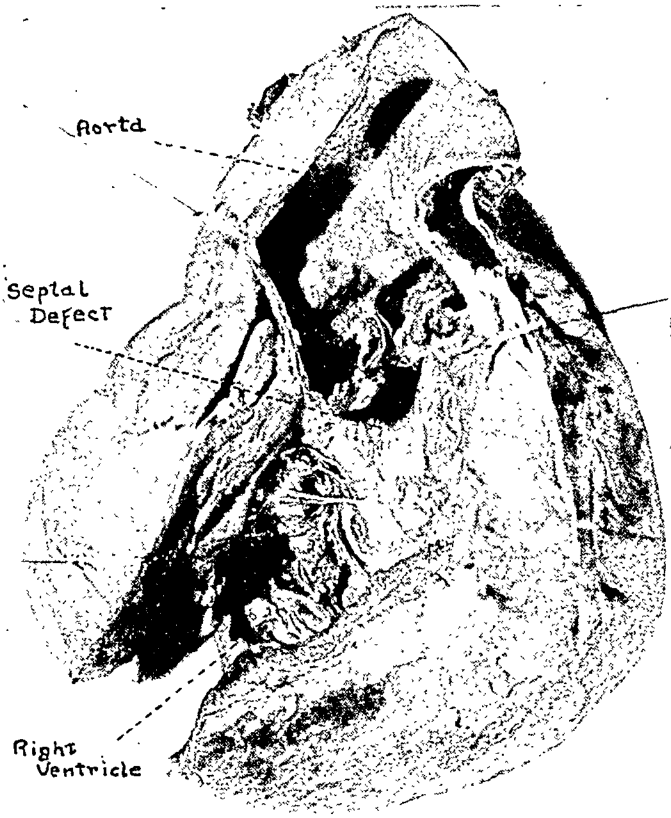

Fig. 5.—Right ventricle opened showing right-lying aorta and interventricular septal defect. Note vegetations on aortic cusps.

posterior to the angle between it and the infundibular cusp, half in the auricle and half in the ventricle" (Abbott).

The tricuspid orifice is directed downward, forward, and to the left. The valve cusps are almost completely destroyed and replaced by great masses of vegetations measuring as much as 15 to 17 mm. in thickness. This luxuriant growth not only invades the valve but also extends well into the musculature of the walls and into the papillary muscles (see Fig. 6).

The musculature of the right ventricle is greatly hypertrophied, averaging 16 mm. in thickness. The right ventricle composes most of the anterior part of the heart. The cavity appears dilated but in form is somewhat flattened and elongated. The cavity is partially divided into two parts by a thick muscular projection running from the anterior part of the interventricular septum, beginning at a

point 2.5 cm. from the apex of the heart, backward, and to the right for a distance of 4.5 cm.; thence it curves forward and downward toward the right to the anterior wall, to be lost in the musculature of the ventricle. This division produces a semilunar orifice about 3 cm. in length and about 1 cm. at its widest point demarcating the conus above from the remainder of the right ventricular cavity below.

Superior to the upper part of this muscular cushion there is a defect in the interventricular septum which admits the index finger. The septal defect, therefore, appears to open into the conus and not into the sinus of the ventricle. The superoposterior part of the conus opens into the aorta. The left inferior part of the conus leads into a small funnel-shaped recess surrounded by thick muscular walls. This latter recess (which, as will be explained later, would appear to represent the lower bulbar orifice) measures 3 cm. below the round margin of the defect in the interventricular septum. This shallow pocket leads immediately into a narrow canal which courses through the thick muscular wall a distance of 6

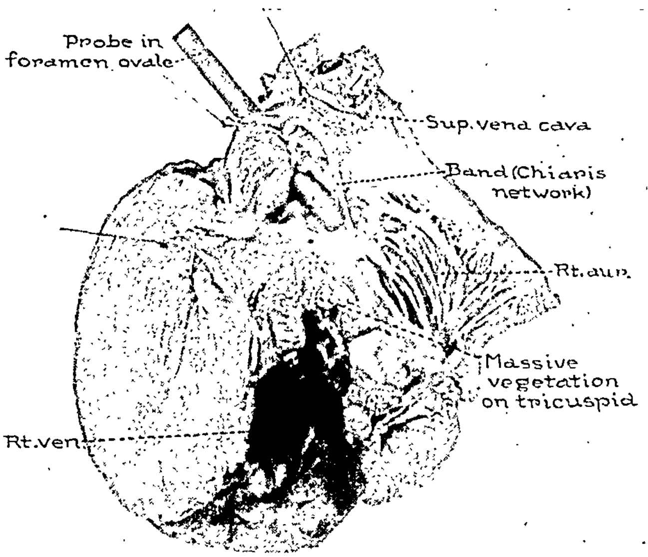

Fig. 6.—Right ventricle and right auricle opened.

mm., thence opening into a larger, thin walled cavity. The channel will just admit a round probe measuring about 3 mm. in diameter. The endocardial lining is thickened but smooth except at its distal portion where there are a few pinhead-sized vegetations projecting from the free surface into the larger cavity. Three cm. above this narrow orifice there are two cusps facing right and left, guarding the pulmonary orifice. These valve cusps are very thin and appear like the valves of a vein. The left cusp is one-third wider than the right. They are free of vegetations (see Fig. 4). The pulmonary artery widens out above these and is situated to the left of the aorta. At its widest portion it measures 3.5 cm. in circumference. The wall appears as delicate as that of the superior vena cava. The ductus arteriosus is completely obliterated. The cavity below the rudimentary bivalvular orifice is conical in form and will just admit the tip of the little finger.

The aorta, as stated above, is continuous with the superior portion of the conus of the right ventricle (see Fig. 5). It rides directly over the interventricular septal defect so that the communication with the right ventricle is about equal to that with the left. The margin of the defect is broad, smooth and shows no sclerosis of the endocardium nor any vegetations. The aortic valves, 2 posterior and 1 anterior, are large. There are fresh vegetations, 5 mm. thick in places,

attached to the ventricular surfaces of the two posterior cusps only, their free margins and their attachments being smooth. The sinuses of Valsalva are capacious. The coronaries arise in the normal manner from behind the left posterior and the anterior cusps.

The condition of "Rechtslage" or right-lying aorta, is made plain by the following anatomical proof.[5] In the normal heart the pars membranacea septi lies at the base of the right posterior aortic cusp and between it and the anterior cusp. In this case, however, it is situated between the bases of the right and left posterior cusps. Thus, the right posterior cusp lies in front of instead of behind, the pars membranacea (see Fig. 6).

The first portion of the aorta measures 6 cm. in circumference. The wall is of normal thickness and the intima is smooth.

The left auricle is small, and its wall is thin; the pulmonary veins open normally into it, three to the right and two to the left. The mitral valve appears normal. The anterior cusp measures 5 cm. and the posterior 3 cm. The margins are not thickened and are free from vegetations.

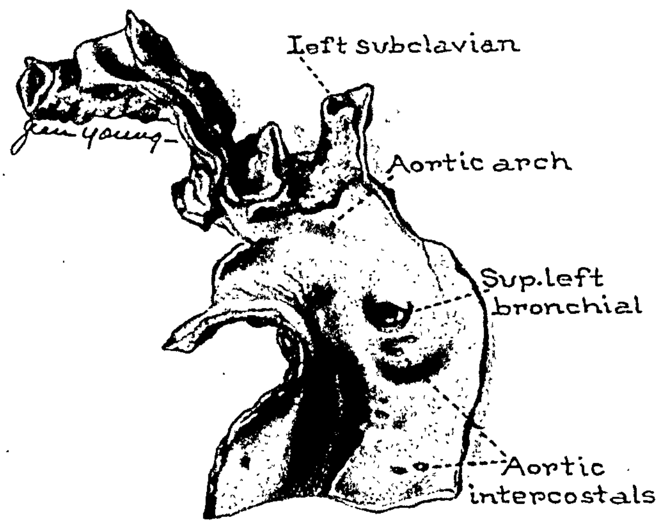

Fig. 7.—Drawing of dissection of upper thoracic aorta showing very large superior left bronchial artery.

The left ventricle makes up less than half the heart in bulk. The cavity is moderately dilated. The wall averages 12 mm. in thickness. The endocardium is smooth and shining. The interventricular septal defect measures 6 cm. from the apex of the cavity. The channel leading from the left ventricle toward the aorta at the level of the septal defect is about the same size as that from the right ventricle. At the rounded borders of the defect the septum measures 11 mm. in thickness (see Fig. 6).

The coronary vessels appear normal as to their size and distribution. The aortic end of the ductus arteriosus is entirely obliterated, and there is no coarctation at any point in the aorta. The branches of the pulmonary artery, though small and vein-like, divide and are distributed to the lungs in a normal manner.

The full collateral circulation to the lung was not worked out at time of autopsy. Later dissection, however, indicated that this was mainly or entirely from the bronchial arteries. Examination of the superior left bronchial arising from the aorta shows it to be from four to five times the normal diameter (see Fig. 7).

Microscopic examination of the heart showed diffuse fibrinopurulent endocarditis and myocarditis with numerous colonies of cocci. There was ulceration of the wall. The heart muscle showed cloudy swelling, Zenker's necrosis, edema and congestion. There were collections of leucocytes throughout the heart which also showed atrophy and fatty degenerative infiltration.

The bacteriological reports from cultures taken at time of autopsy were as follows. No growth was obtained on culture of the heart's blood after five weeks' incubation. From the vegetations on the tricuspid valves, however, streptococcus viridans was found on culture.

DISCUSSION

Pathological Anatomy.—The most striking finding was the extreme degree of stenosis of the pulmonary conus, which measured only about 3 mm. in diameter (see Fig. 6). The narrowing was so marked that it might almost be classified as an atresia, as, indeed, very similar cases are described by early authorities. In an atresia reported by Weiss and quoted by Abbott[4] "the conus admitted only a pinhead or a fine straw, and was lined by thickened endocardium; above this were two fairly large pulmonary cusps, and the artery itself was comparatively large. There was a small patent foramen ovale, a large defect of the septum at the base and a large thick walled aorta arose from the right ventricle above the defect." His case was evidently very similar to this one.

The condition of the conus and its relation to the rest of the right heart resembles that in Case 3 described by Abbott, Lewis and Beattie.[6] "The conus is as large as, or larger, than normal but is completely aplastic above and is demarcated below from the sinus of the right ventricle by the hypertrophied muscle bands (crista supraventricularis and trabecula septum marginalis) which mark the site of the lower bulbar orifice of the embryonic heart, thus representing the condition described by Keith as "conus a separate chamber." They make the anatomical conclusion that "in pulmonary stenosis or atresia with septal defect the condition of the conus of the right ventricle, whether hypoplastic or not, will depend upon whether the defect in the septum opens into the sinus of the ventricle or into the conus. In the former case the conus will be small and aplastic; in the latter it will be large and thick walled." As already seen from the description the present case appears to follow this rule.

Another anomaly in the heart quite distinct from the tetralogy of Fallot was the presence of an anomalous network in the right auricle (see Fig. 6). This condition was first described on the basis of eleven original cases by Chiari[7] as a delicate fenestrum extending from the Eustachian valve across the cavum of the right atrium. Heuper and Berghoff[8] added two cases and state that in all seventeen cases have been described. Another one, an extensive network, was seen recently by the writer in a case showing no other anomalies. Chiari came to the conclusion that the network is a definite developmental anomaly, the

threads being residues of the valvula venosa dextra and of the septum spurium. Such a condition is not entirely without clinical significance. Although these strands may exist without giving any evidence of their presence, the fine reticulum in the right auricle may supply a possible nidus for thrombotic processes, which may lead to embolism (Abbott).

The vegetations at the site of the tricuspid valve presented a remarkable appearance on account of their great size, measuring as much as fifteen to seventeen mm. in thickness. The cusps were almost entirely destroyed. The process extended to the walls of the ventricle and caused ulceration. There was even a fibrinopurulent myocarditis as well as endocarditis, and microscopic examination showed numerous colonies of cocci in the deeper layers.

Just here some reference should be made to the bacteriological studies in this case. Repeated blood cultures during life were negative. Also cultures of the heart's blood taken at autopsy showed no growth. But cultures taken from the vegetations themselves produced an abundant growth of Streptococcus viridans. In view of the very severe infection and the evidences of septicemia in the heart and elsewhere in the body it seems remarkable that the heart's blood should be sterile. As accurate statistics on conditions such as this are difficult to procure, no conclusion is drawn, but the possibility is suggested that the same factors responsible for the production of such luxuriant vegetations have the effect of inhibiting growth in the blood stream. Most inflammatory processes involving the right heart seem to be due to the pneumococcus or other microorganisms of higher virulence than the Streptococcus viridans.

The extravagantly fungating character of the vegetations in right-sided lesions where there is a septal defect has been noted and studied by Abbott.[9] No satisfactory explanation has been found to explain why such vegetations surpassing anything ever seen in the left heart should occur here. It is of significance, however, that such a condition occurs in the presence of an arteriovenous shunt. From this fact Boldero and Bedford[10] have suggested that the presence of the oxygenated blood which enters through the defect may be the cause of this redundancy. Abbott thinks this commingling may be indirectly responsible, but that a lessened oxygen unsaturation of venous blood would not alone account for it, since we do not see this rate of growth in vegetations in the left heart in which aerated blood continually flows. Working on this hypothesis and noting the situation of the lesions, the present case helps to illustrate the direction of intracardiac flow in the presence of the septal defect. The tricuspid valve was involved most of all. Throughout the latter part of the disease it must have been incompetent to a greater or less degree, so that the mixed blood flowed back over the cusps. The aortic cusps were involved less, and there were only a few minute vegetations attached to the thickened endocardium at the site

of the conus stenosis. The pulmonary cusps and the entire left heart were free.

It is important to note the parts of the heart involved by the endocarditis because here is additional proof that such processes occur in tissues which for various reasons have become predisposed to this type of infection. The influence of wear and tear in producing *locus minoris resistentiae* is undoubtedly great. A second well-recognized factor is the presence of local deformities, upon which also the first factor may depend. The tricuspid valves must have been the sites of unusual stress and strain. In Abbott's series the highest frequency of this infection was on malformed cusps. In this case the pulmonary valve was exempt, doubtless because it never functioned to any great extent. But the thickened endocardium of the conus opening was the seat of vegetations. Next to deformed valves the commonest site is a septal defect. The margins of the defect in this case, however, were clear, probably on account of the fact that they were not sclerotic. An important predisposing factor is the location of a defect in close proximity to valvular endocardium where there is an area of sclerosis. Thus, endocarditis does not occur around defects in the upper part of the interauricular septum or where the entire interventricular septum is absent.

Associated Anomalies.—It has long been known that congenital defects, particularly those classed definitely as due to arrest of growth, are apt to be multiple in the same individual. Anomalies elsewhere occur so frequently in congenital heart disease that this gives strong support to the view that a common cause is responsible for all. In Abbott's series of 850 cases 17 per cent showed associated anomalies. This association is too frequent to be considered accidental.

In the present case it is interesting to note the multiplicity of anomalies apart from those found in the heart. These conditions aside from the mental deficiency were confined to skeletal deformities.

1. Mental deficiency. The patient had always been considered below par in intelligence. Abbott states this to be not infrequent, although intelligence is sometimes even higher than the average, as instance the case of Gilbert, the composer.

2. Inferior degenerative constitution. This refers to the general type, build, facies, etc. The patient was a slender asthenic type with a long, narrow head and distinct brachygnathia.

3. Asymmetry of the calvaria. This was manifested by a depressed area slightly more to the right in the occipitoparietal region. Such an anomaly was noted by Dr. Abbott in her series.

4. Bilateral cervical rib. The one on the right side articulated at its tip with the first rib. The left was free.

5. Partial suppression of twelfth ribs. Both were very short.

6. Scoliosis.

The underlying cause of such arrests and disturbances of growth still remains obscure. It is generally thought that it is not due so much to a hereditary predisposition as to some constitutional disturbance or disease in the maternal tissues or fetal envelopes, that is, in the environment of the developing embryo. It seems of some significance that the patient in this case was the last child of a family of eight, her mother and father being aged 47 and 56 respectively when she was born. Instances such as this of the occurrence of congenital cardiac defects in children of parents who have both reached middle life have been observed before. Abbott notes the striking parallel in Mongolian idiocy which also occurs usually as an "exhaustion product" of elderly parents, and as the last of many pregnancies.*

Pathological Physiology and Clinical Aspects.—As pointed out by Abbott, Fallot's tetralogy supplies the best example of the "immediate and remote effects of a high degree of oxygen-unsaturation persisting throughout many years. It illustrates the combined effect of a permanent venous-arterial shunt of the circulation through the septal communication as a result of the raised pressure in the right ventricle, and of an increased deoxygenation in the systemic capillaries from retardation of the flow there." All the classical features of this morbus caeruleus, cyanosis, clubbing, dyspnea and polycythemia are the expression of deficient aeration of the blood. Most striking of all is the cyanosis which differs from the cyanosis of later stages of acquired heart disease in that it may exist for many years without any signs of cardiac insufficiency.

The exact explanation of the cause of the cyanosis was long a subject of controversy. Early writers attribute it variously to the following: (1) venous stasis; (2) admixture of venous with arterial blood; (3) deficient aeration; (4) dilatation and new formation of capillaries in the lungs; (5) peripheral parts of the body; (6) changes in the blood itself, i.e., polycythemia. Abbott traces the progression of these views up to the light of our present knowledge and shows how each of the theories contained a part but none the whole of the truth. It remained for Lundsgaard and Van Slyke[11] to clarify and explain the condition in their very important monograph. This work has been of great value in distinguishing the essential causative factors from the modifying ones. A discussion of the present view would be too lengthy for the scope of this paper; but to quote Abbott, it may be summarized by saying that the dependence of congenital cyanosis upon deficient

*At the time of writing, a case of a twenty-two months old male child came to autopsy at the University of Michigan Hospital showing an anomalous, distorted right posterior aortic cusp and double right coronary. Associated anomalies were macrencephaly, hydrocephalus, anomalous lobation of both lungs, absence of left temperomandibular joint, anomalous external ear, accessory auricle, anomalous maxillae, and a sacrococcygeal dimple. Of the last three autopsied cases of harelip, two showed cardiac anomalies, one a cor biatrium triloculare and cor biventriculare triloculare. There is now a patient, a female, aged 28 years, under observation in the department of medicine, with a diagnosis of mild pulmonary stenosis who has also an anomaly of the urethra.

oxygenization is now definitely established. According to Warthin,[12] however, Abbott fails to recognize sufficiently the important recent work on capillary morphology and pathology bearing directly upon the question of morbus caeruleus. He cites the work of Redisch and Rösler which presents an entirely new aspect to morbus caeruleus by their findings of a constant capillary dilatation which they consider to be the cause of the affection. The circulation evidently accommodates itself to a certain degree of oxygen-unsaturation, whether brought about by obstruction in the course of the pulmonary artery, by general retardation of flow, or by a mingling of venous with arterial blood; but as soon as deficient oxygenization reaches a certain limit, this becomes insufficient for the needs of the body, and cyanosis results. Thus, in the present case, the patient was always much bluer upon exertion. Yet in spite of the obvious severe grade of anoxemia, she was able to undertake fairly severe muscular exertion. This power of adaptation is remarkable. It may be considered analagous to the gradual acclimatization of individuals to the anoxemia produced by the lowered oxygen tension of the atmosphere in high altitudes.[4] As in polycythemia vera, the red cell count is raised. In this case it was 7,450,000. Counts as high as 12,000,000 have been reported. In this connection it might be of interest to note that such a high degree of viscosity of the polycythemic blood may sometimes produce a temporary thrombosis of the cerebral capillaries (Abbott) and give rise to curious epileptiform attacks. This doubtless explains symptoms in the case of Gilbert, the musician, already referred to. He was subject to dizzy spells and frequent headaches. Sometimes he was "thought to be intoxicated because he staggered in a faint spell." And later in his life there were "attacks resembling transient apoplexy, with weakness of the arm, hand or leg for a few hours or a few days, apparently passing off completely."

Oxygen-unsaturation and other blood findings are so characteristic that it is possible to diagnose a congenital heart lesion on these alone. In the recent German literature Uhlenbruck[13] reports a case confirmed by autopsy, where a diagnosis of pulmonary stenosis with interventricular septal defect was made purely on a basis of oxygen deficit in arterial blood, definite clinical symptoms, e.g., significant murmurs, being absent.

The characteristic dyspneic attacks seem to be caused by, and in proportion to, the ischemia of the pulmonary circulation.

Clubbing of fingers and toes, a prominent symptom, seems to be caused chiefly by stasis and lack of oxygenated blood with consequent effects on the tissues due to toxic products of metabolism which escape oxygenation. In this case there was chronic periosteitis but no new formation of bone.

With regard to the degree of disturbance of the circulation several factors must be considered. The degree of narrowing, whether simple

stenosis or complete atresia, is of prime importance. But one cannot judge the seriousness of the lesion from this alone. The seat and character of the stenosis and the presence or absence of an interventricular septal defect are also factors, so that in pulmonary stenosis an associated septal defect is unfavorable because its presence tends to reduce the volume of blood passing through the stenosed orifice and to permit the passage of venous blood into the arterial stream. But in atresia, where life is usually very short, an associated septal defect facilitates aeration, and there is less cyanosis and a better prognosis.[4] The present case falls into the class of extreme stenosis. From the standpoint of age attained, 16 years, it is unusual. In Abbott's series the average duration of life in all cases of pulmonary stenosis with defect of the interventricular septum was 10.8 years, and in atresia 3.4 years. In this case, besides the extreme conus narrowing other factors contributed to the seriousness of the lesion. There was a patent foramen ovale, the presence of which is unfavorable, probably because a smaller volume of blood is transmitted directly to the aorta. Also, the absence of a patent ductus arteriosus necessitates the blood supply to the lung proceeding by an even more devious route, a point to be discussed shortly.

In cases like the present one, it does not seem unreasonable to assume that the stenosis becomes relatively more marked with the growth of the heart after birth. With the establishment of a more or less efficient collateral circulation to the lungs the functional importance of the pulmonary conus becomes less. There is a decreased tendency for the passage to enlarge in proportion to the growth of the rest of the heart, especially as the rudimentary channel is lined by thickened endocardium surrounded by the heavy musculature of the right ventricle, which of necessity must develop a functional hypertrophy. In stenosis of a more distal part of the pulmonary tract, i.e., the artery at or above the valves, or one of the branches of the vessel, there is a tendency for the lumen to enlarge owing to the force of the blood on a thin walled structure, not as in the conus deformity surrounded by the constantly constricting musculature of the heart. Therefore, in marked conus stenosis, as time goes on, the relative functional importance of the pulmonary artery becomes less according to the degree and situation of the malformation. The lumen remains small, the walls thin and the valves delicate. In atresia the artery may be represented merely by a thin cord, as in the type well illustrated by Keith.[5] This relative progression of the anomaly would seem to be the chief factor to explain why it is that the majority of cases show few, if any, symptoms and no cyanosis at birth. Commonly this characteristic sign in morbus caeruleus becomes evident only after several weeks, months or, as is frequently the case, years after birth. Subsequently, cyanosis tends to increase rather than diminish. Thus, to instance the present case, the degree of stenosis at the age of 16 years was so extreme as to be almost an atresia and physiologically

must have acted practically as such; but earlier in her life the same sized opening would have permitted a relatively more normal pulmonary circulation. As the heart grows, the marked stenosis acts more and more like an atresia. If life be maintained, it is obvious that the compensatory or accessory pulmonary circulation is of prime importance. A brief consideration of this may be of interest.

Collateral Pulmonary Circulation.—When a widely patent ductus arteriosus persists, as is usual, the problem is simple. The blood flows from the right ventricle through the aorta a short distance and is distributed to the lungs by way of the ductus through the distal pulmonary radicals. But in many cases this fetal passage either does not persist or is not large enough to supply the needs of the lung, which must then rely largely on vessels separate from and not communicating with the main pulmonary stems.

A consideration of this is omitted or neglected in much of the literature on congenital pulmonary stenosis. Meckel was the first to suggest that in these cases the dilated bronchial arteries might carry on this function. Then Küttner[14] in 1878, proved by experiment that a very free anastomosis does normally exist between pulmonary and bronchial circulation in the lungs. His conclusions were disputed by some workers. Miller[15] in 1906, on the basis of experimental lung injection denied the existence of an anastamosis between the two systems. Others, however, have strongly supported the view of Küttner, notably Königstein.[16] But in the normal lung there is probably not as free a communication as Küttner at first thought. There is a very rapid breaking up of the pulmonary artery into capillaries. But unless almost the entire pulmonary supply to the lung is cut off, there is sufficient anastomosis with other branches of the pulmonary to compensate without the aid of the bronchials. Ghoreyeb and Karsner[17] have shown that the pressure in the pulmonary radicles must reach a very low level before the bronchial circulation is brought into service to compensate. Thus it would appear that the blood from the bronchial tree reaches the alveolar capillaries of the lung only in the greatest emergency when there is severe embarrassment of the pulmonary circulation. When this occurs, as in marked congenital pulmonary stenosis, the demand is urgent, and being present early in life, the bronchial arteries the more readily become enlarged and adaptable. The most extensive work bearing on this seems to be in the German literature, notably that of Christeller.[18] Searching the records of congenital pulmonary stenosis and atresia with closed or deficient ductus where the collateral pulmonary circulation was reported, he listed 26 cases, going back over a hundred years. Analysis of this shows that the bronchials were the *most important*, although sometimes other arteries shared or entirely assumed this special duty. He classified the vessels which may constitute the compensatory circulation as follows: (1) patent ductus arteriosus; (2) anterior bronchials; (3) posterior

bronchials; (4) anterior mediastinals; (5) posterior mediastinals; (6) esophageal; (7) pericardials; (8) coronaries; (9) anomalous arteries (e.g. from the aorta itself or from the subclavians).

In the present case it appeared that the bronchial arteries supplied the collateral circulation. Fig. 7 shows a portion of the thoracic aorta with the much enlarged superior left bronchial coming off just above the first paired aortic intercostals.

Christeller observed that a marked stenosis acts like an atresia, and he also points out that most patients die from intercurrent causes and not from insufficient circulation or heart failure.

Clinical evidences of an advanced subacute bacterial endocarditis were apparent in the case under consideration as soon as the patient came under observation. These accentuated rather than masked the congenital heart lesion. Cyanosis was very marked. Dyspnea was present. The loud rasping systolic murmur and other physical signs were pronounced.

The x-ray plate showed a relatively large, hypertrophied right ventricle. Owing to the serious condition of the patient only an antero-posterior plate was taken with a portable machine. This did not show the shadow of a second left arc which Abbott states is usually present, being due to the greatly hypertrophied conus of the right ventricle. The electrocardiographic tracings showing marked right ventricular preponderance were characteristic for cases of pulmonary stenosis. This preponderance was much in excess of that shown by any acquired lesion such as mitral stenosis.

There was surprisingly little dyspnea and orthopnea considering the very advanced vegetative endocarditis superimposed upon a heart already functioning under great difficulties. In spite of the extreme cyanosis the patient showed few signs of congestive heart failure. Hers was a "warm cyanosis." The heart compensated extraordinarily well until the bacterial infection overpowered it and, as demonstrated post-mortem, invaded and ulcerated the heart muscle as well as the valves. This bears out the statement that most patients die from intercurrent causes and not from cardiac failure. This girl had a marked susceptibility to infection. She had had in addition the usual infectious diseases of childhood and smallpox. Reference has already been made to chorea from which she suffered about two years prior to her death. Some time prior to the onset of her fever and acute illness she had three teeth pulled. This seems of particular significance as pointing to a possible focus, the starting point of her final overpowering infection. In the examination of records of these cases it is striking how often infective foci precede death.

Fallot established the fact that a diagnosis of these cases could usually be made during life with a fair degree of certainty. The decided localization of murmur and often thrill, the increased cardiac dullness to

the right, the absence of pulmonary accentuation, and the presence of distinctive symptoms of congenital cyanosis, clubbing, dyspneic attacks, etc., often make possible a positive diagnosis. Patent ductus may give very similar signs, but in the latter there is usually pulmonary accentuation. The electrocardiogram and other methods mentioned previously are of course of much aid in diagnosis.

The prognosis in congenital heart disease is notoriously poor. It is, however, extremely variable and is affected by many factors. It depends first of all on the direct effect of the lesion upon the circulation and, consequent to this, the degree of oxygen unsaturation in the blood. In pulmonary stenosis with septal defect adult life is seldom attained, even with stenosis of a comparatively mild degree. The type in which the septum is closed gives a better prognosis. On the other hand with pulmonary atresia (and this case may almost be considered as such), the presence of a septal defect gives a relatively better prognosis than if it is closed. Yet even here nearly all patients die in early childhood. In Abbott's series the maximum age with pulmonary atresia, interventricular septal defect and patent foramen ovale was eleven years. The present case, therefore, although not strictly an atresia, would appear to be exceptional. Symptoms are a better guide to prognosis than physical signs. For example, a septal defect may give a marked murmur and thrill, yet lead to no hampering of the heart's action and to little interference with oxygenation, until some additional factor, such as obstruction in the pulmonary circulation, intervenes, producing a transient or terminal cyanosis. Persistent cyanosis, a continued low temperature and a high red cell count indicate a poor outlook (Abbott). Endocarditis is the gravest danger to all those who reach adolescence or early adult life.[9] And particularly is it so for such as the present. The danger of cerebral complications is greater than generally supposed. This is well brought out by Abbott,[6] who shows the great frequency of paradoxical embolism. In the case of Gilbert, cited above, who died of "apoplexy" with hemiplegia, death was due very likely, it is suggested, to this phenomenon, particularly as he had had repeated attacks suggesting embolism and since his blood pressure was always low and his arteries soft.

Another possible factor in the prognosis which, although not specifically mentioned by Abbott or others, seems to me of some significance is the collateral pulmonary circulation. In cases of marked stenosis or atresia, it would seem of considerable importance just where the lungs got their blood supply and how efficient this accessory circulation had become. For, as pointed out above, the route is much different when the ductus is closed.

It follows from what has been said about the danger of infections that patients with this disease must be carefully guarded against them. The social and economic factors must therefore of necessity be important

because where good hygiene prevails and the most suitable conditions of living are instituted the outlook is better.

SUMMARY

A clinico-pathological study has been made of a case of congenital heart disease exhibiting the complex known as the "tetralogy of Fallot," upon which was superimposed a subacute bacterial endocarditis with massive vegetations involving chiefly the tricuspid valve. Associated anomalies in both the heart itself (Chiari's network) and elsewhere have been discussed with reference to their bearing on the theories of the etiology and pathogenesis of congenital cardiac defects.

Special reference has been made to the collateral pulmonary circulation in the presence of extreme pulmonary stenosis or atresia when the ductus arteriosus is closed. A consideration of this has been neglected in most of the literature on congenital pulmonary stenosis. In such cases the enlarged bronchial arteries usually supply the blood to the lungs, although sometimes the pericardials, mediastinals, coronaries, esophageals, subclavians, or other arteries are called upon to assume this function. In the present case the bronchial arteries were greatly enlarged.

Aspects of the pathological physiology in the case are discussed with reference to the degree of disturbance of the circulation and its relationship to prognosis. The danger from infections is noted, particularly the extraordinary forms of vegetative endocarditis to which such cases are especially prone. Most patients die from intercurrent diseases and not from cardiac failure.

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Department of Clinical Reports

THE ELECTROCARDIOGRAMS OF CORONARY OCCLUSION FOLLOWING A STAB WOUND IN THE LEFT VENTRICLE

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THE surgical aspects of this case were reported by Dr. Bates before the Philadelphia Academy of Surgery, January, 1929, and published in the Annals of Surgery, April, 1929. We will use his report and the further hospital records in summarizing briefly the history of this patient, and then present the electrocardiograms taken at weekly intervals, beginning five days after the injury and ending when they have returned to his normal.

CASE REPORT

A young negro, 28 years old, was admitted to the accident ward of the Graduate Hospital at 1:15 A.M., on November 15, 1928. He had an incised wound in the anterior aspect of the left chest underlying a cut in the lapel of his coat, his vest, shirt and undershirt. The wound in the chest wall was about 1½ inches long, was vertical and just to the outer side of the left border of the sternum.

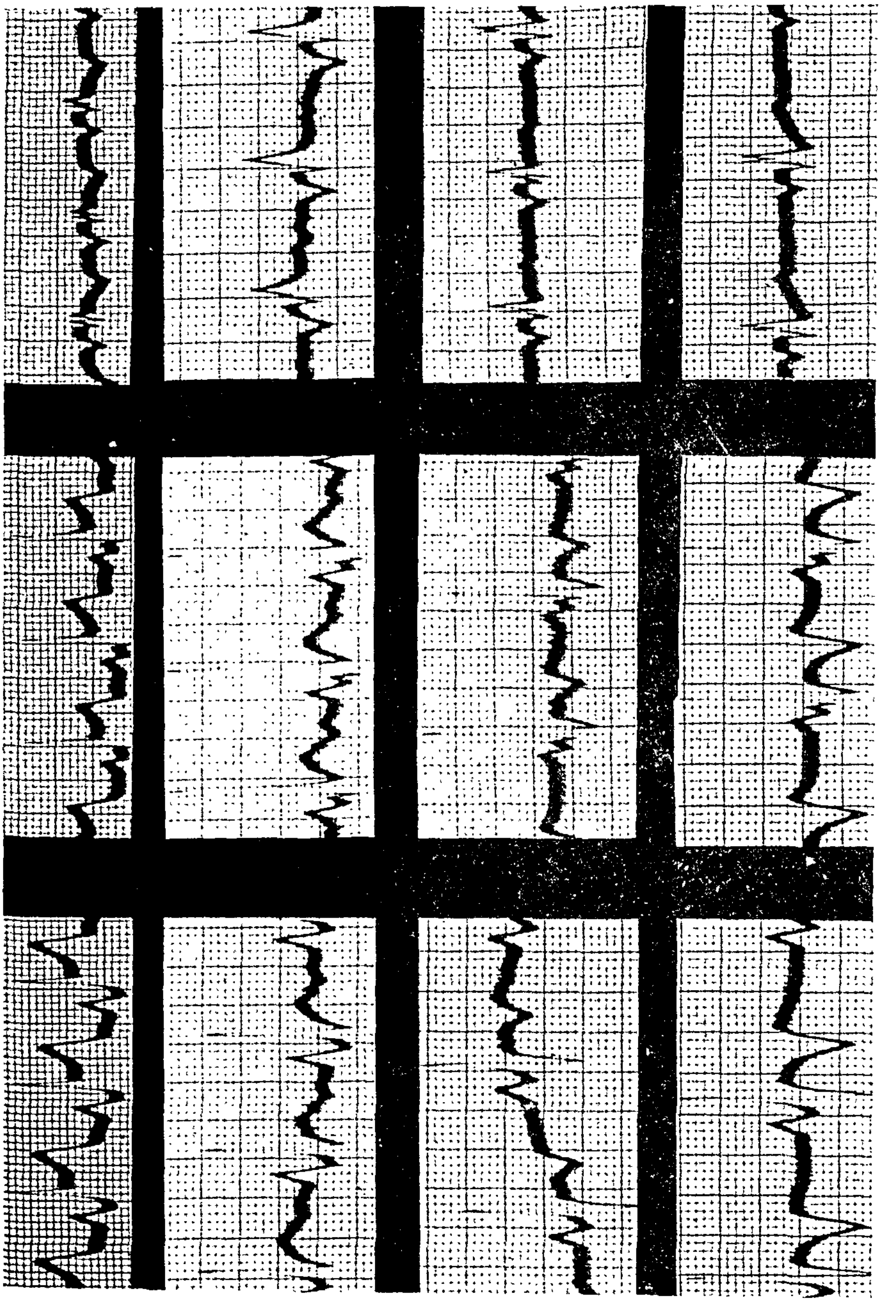
On admission the patient's temperature was normal, and his pulse 48. There was a loss of blood, but not large. The heart sounds showed a curious scraping or catching in the rhythm. The pulse rate quickly mounted, and the area of cardiac dullness rapidly increased, so that it was deemed advisable to explore the wound.

The vertical incision was enlarged upward and downward, and it was found that the knife had passed through the costochondral junction of the third and fourth left ribs. The intercostal muscles between the second and third, fourth and fifth ribs were severed, and the ribs were broken about 2 inches from their traumatic detachment. When an osteoplastic flap was laid back, the opening in the pericardium was easily seen. Bleeding was steady, and it was seen to be blood pumped from within the pericardium rather than from a cut vessel in the edges of the pericardium. Hemostats were applied to the two edges of the stab wound, and the pericardial opening enlarged upward and downward. Sponging cleared the field so that a hole in the left ventricular wall was visible over toward its right boundary and near its upper border. The knife blade had just missed the left coronary and its descending and circumflex branches, but it may have severed one or more of their branches in the heart wall. It was impossible to determine whether or not the wound connected with the left ventricular chamber, but from the amount of bleeding it was judged either that it did not, or else that there was a very small opening. The muscular bleeding was very steady, and with each contraction and rotation of the heart there was a steady spray of blood carried in the form of an arc on the table drapings above the wound.

Lead III

Lead II

Lead I

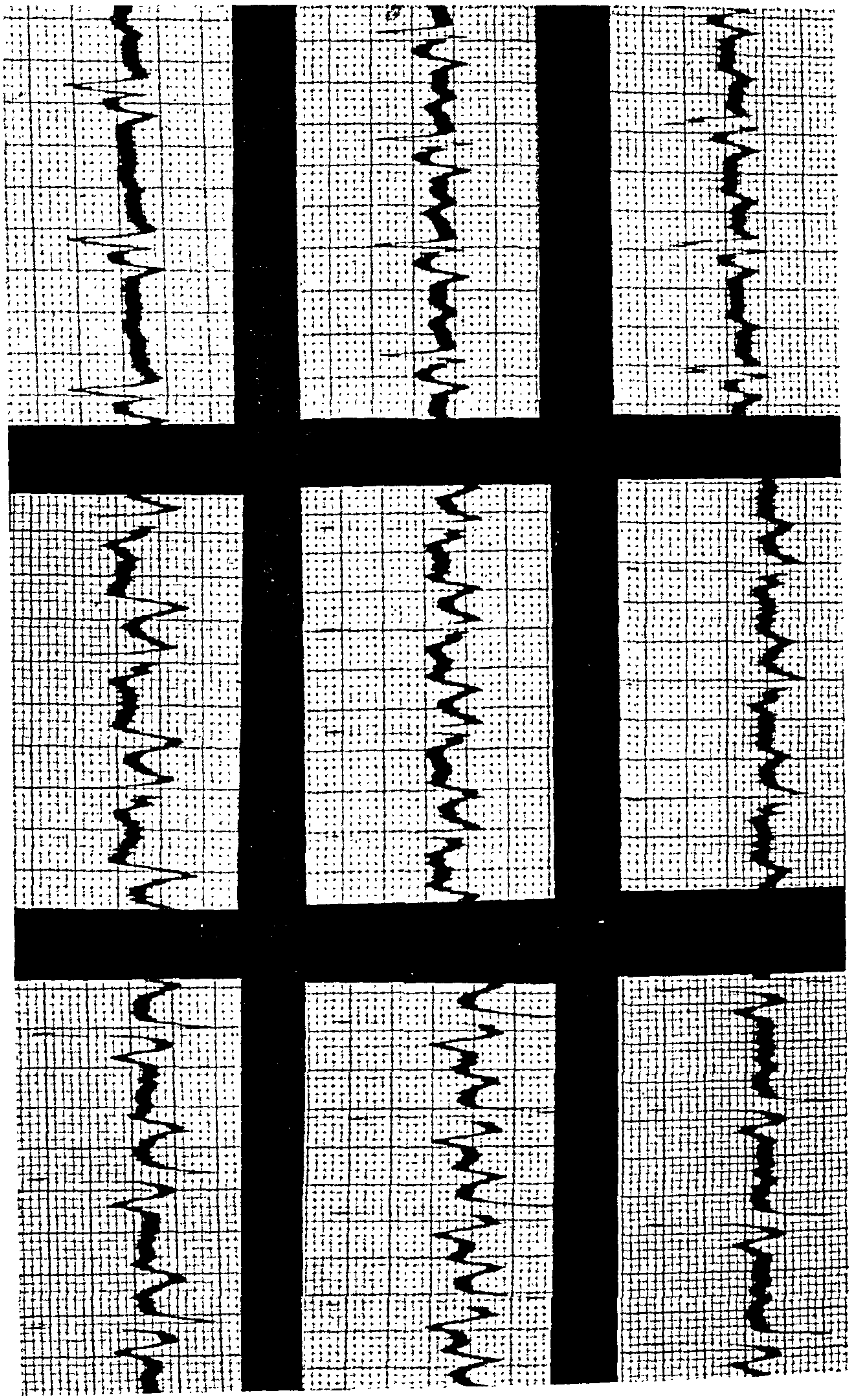


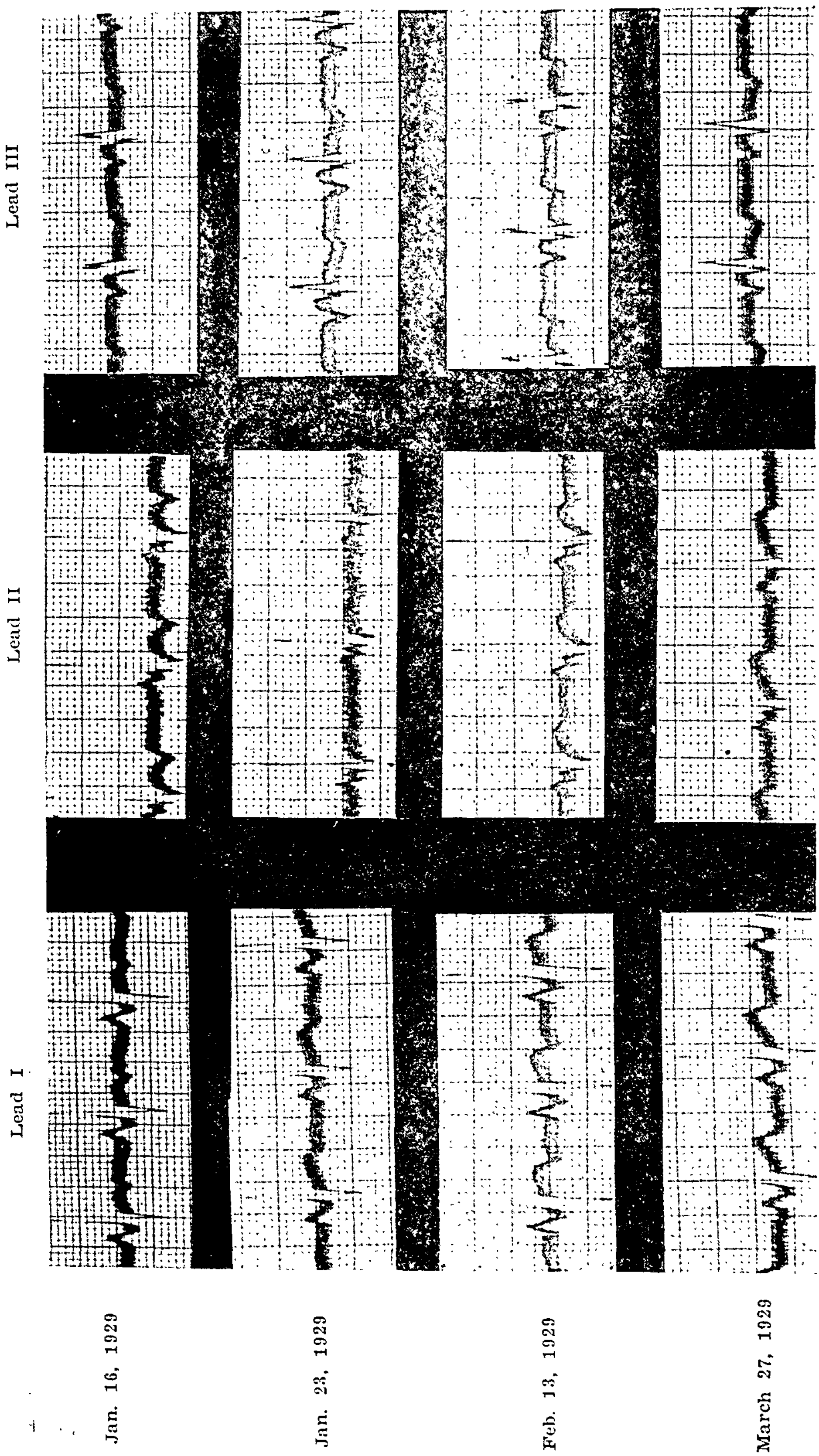
Nov. 20, 1928

Nov. 27, 1928

Dec. 5, 1928

Dec. 11, 1928


Lead I
Lead II
Lead III
Dec. 17, 1928
Dec. 27, 1928
Jan. 10, 1929


Lead I
Lead II
Lead III
Jan. 16, 1929
Jan. 23, 1929
Feb. 13, 1929
March 27, 1929

The wound in the ventricle was closed with a mattress suture. Following this a running suture was placed in the cut epicardium. The pericardium was then washed out with normal saline, and as the pericardial wound was being closed the heart stopped. It was slightly massaged by a finger through the wound, and 10 minims of a 1:1000 adrenalin chloride solution were given intramuscularly. Intravenous normal salt solution was then started. The pericardium was about closed when the heart again stopped. It was gently stroked by a finger inserted through the lower angle of the pericardial incision, adrenalin was run in with the intravenous saline, the heart rapidly recovered its normal rate, and there was no further trouble. Following this the external wound was closed.

During the time on the table the pulse rate never went over 108. The patient was in the hospital 27 days. His leucocyte count immediately following the operation was 10,200; and just prior to his discharge, 10,400. About ten days after the operation there was an exacerbation of fever, and the leucocytes rose to 19,000. At this time there was a pericardial friction rub and increase in the area of heart dullness. That there was pleuropericardial inflammation was also suggested by evidence of fluid at the left base. Soon after the development of the pericardial friction rub on November 26, 1928, the x-ray report showed a cardio-thoracic ratio of 19.5 : 29 cm., the left base line measuring 12.5 cm. The cardiac shadow showed general enlargement, but especially to the left. The left border of the heart appeared somewhat straightened, which may have been due to pericardial effusion; the aorta was not markedly enlarged, and the lungs showed no marked changes.

On December 1, 1928, the cardio-thoracic ratio was 15.5 : 28 cm. There was a marked diminution in the size of the cardiac shadow, and the lungs were clear.

On January 18, 1929, the cardio-thoracic ratio was reduced to 13.5 : 28.8 cm., which was apparently its normal.

The Wassermann and Kahn reactions were strongly positive in this patient, but he showed no evidence of change in aorta or valves, so that the lues was probably a comparatively recent event. The urine, the blood and blood chemistry were normal.

He was discharged to the out-patient clinic on December 12, 1928, but has been kept under constant observation since, and had an electrocardiogram taken weekly. At the present he shows no cardiac enlargement and no murmurs. There is no friction rub, but after exertion there is evident pulsation in the third and fourth interspaces adjacent to the left edge of the sternum, which suggests the possibility of some slight adhesions in that region. His blood pressure averages about 120 mm. systolic and 70 mm. diastolic. The heart rate and rhythm are normal. He feels well, and he has been doing light work around the hospital since his discharge.

A series of electrocardiograms are given showing the changes that went on from week to week until what appeared to be his normal curve had returned.

The first one was taken on November 20, 1928, five days after the injury and operation. In Leads I and II the T-wave came off high above the iso-electric line, and the curve was a typical picture of *acute* coronary occlusion.

In the curve taken November 27, 1928, Leads I and II showed the R-T interval started below instead of above the iso-electric line, but was still circumflex upward. Following it, the slight dip downward

in Leads I and II showed the beginning of the inverted T-wave of *chronic* coronary occlusion.

In the curve of December 5, 1928, Leads I and II showed the well-developed inverted T-wave of chronic coronary occlusion, which reached its maximum in the curve of December 11, 1928, and then began to decrease. The inverted T-wave disappeared more rapidly in Lead I than in Lead II, as was noted in the curves of January 10, 1929, and the following curves. The curve of March 27, 1929, apparently was his normal curve. The electrocardiograms have been taken every week since that time until July, and they have never varied essentially. Lead III has always shown the inverted P and T.

SUMMARY

The young man had a stab wound in the base of the left ventricle, in the region of the main branches of the left coronary artery. The wound was closed surgically, and he made a complete recovery. The first electrocardiogram, taken five days after the injury, was that of *acute* coronary occlusion. The second curve, taken twelve days after the injury was intermediate between the acute and chronic coronary occlusion. Twenty days after the injury T_1 and T_2 showed the typical inverted T-wave and circumflex upward R-T interval of *chronic* coronary occlusion, which reached its maximum twenty-six days after the injury; after this time the inverted T_1 and T_2 began to recede and had reached the normal upright T on March 27, 1929, that is, eighteen weeks after the wound and operation.

PULMONARY STENOSIS WITH BACTERIAL ENDOCARDITIS IN AN ADULT*

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CASE REPORT

CHIEF COMPLAINT.—A woman, 32 years old, was first seen on March 12, 1925, complaining of the fact that all her life she had been unable to play games or hurry without dyspnea, and for the past year this dyspnea had increased in severity and frequency. She also complained of lack of energy and inability to sleep.

Family History.—Negative, except that her husband had died of tuberculosis.

Past History.—She had had measles, chicken pox, mumps and a severe attack of scarlet fever. She had pneumonia when a year old. The family doctor also told her parents that she had heart trouble when she was a year old. At fourteen years of age she had rheumatism. No detailed history of this was obtained. There was no history of tonsillitis or chorea. She had had a chronic cough for years but no expectoration or hemoptysis. Her appetite was poor. There was also an irregular menstrual history. There had been one normal pregnancy.

Present Illness.—She had always been troubled with dyspnea on slight exertion as long as she could remember, and for the past year this dyspnea had increased in severity and frequency. No edema, palpitation or precordial pain was ever present. She had never noticed anything peculiar about her color. Her other complaints at this time were lack of energy and inability to sleep. In the past year she had lost 26 pounds and had not felt particularly well since two wisdom teeth had been removed some months previously.

Physical Examination.—Positive findings: The patient was a thin, pale blond woman. The veins of her neck were distended. On percussion the heart was moderately enlarged, the apex was visible just outside the nipple line, with a marked apical pulsation and a definite thrill over the mitral area. The rhythm of the heart was perfectly regular; the rate 92. There was a loud blowing systolic murmur over the entire precordium, most marked over the pulmonic area, transmitted to the left. At times a presystolic murmur was heard over the mitral area. The systolic pressure was 110 mm. and the diastolic 70 mm. The liver was felt two fingers below the costal margin. At this time the red blood cell count was 6,300,000; white blood cells 8,000; hemoglobin 70 per cent. The chemical examination of the blood was normal.

The electrocardiogram showed normal sinus rhythm. The conduction time was normal. Very marked right ventricular preponderance was present. The P-wave was abnormally large and the T-wave was inverted in Leads II and III.

The Wassermann reaction of the blood was negative, and the urine examination at this time was completely negative.

A radiographic examination of the chest at this time showed moderate hypertrophy of the pulmonary arc and of the right and left sides.

*Presented, in abstract before the Annual Meeting of the New York Pathological Society, at the N. Y. Academy of Medicine, January 10, 1929.

Clinical Course.—The patient went to California in September, 1927, where she had restful out-of-door life, but her cardiac reserve was noticed to be considerably less. When she returned in February, 1928, it was noticed that her dyspnea had increased and that her pulse was more rapid—rate 120. Also she was extremely nervous at this time. She was seen several times during February and complained a good deal of a hacking cough.

On March 1, 1928, she was carefully examined, and at this time her spleen and liver were easily felt. She went to Florida where she stayed about six weeks. At this time she was not sleeping so well, and her reserve had greatly decreased. She was able to do very little except to remain quiet and out of doors. She then went to Atlantic City where she was put to bed for a cough. It was

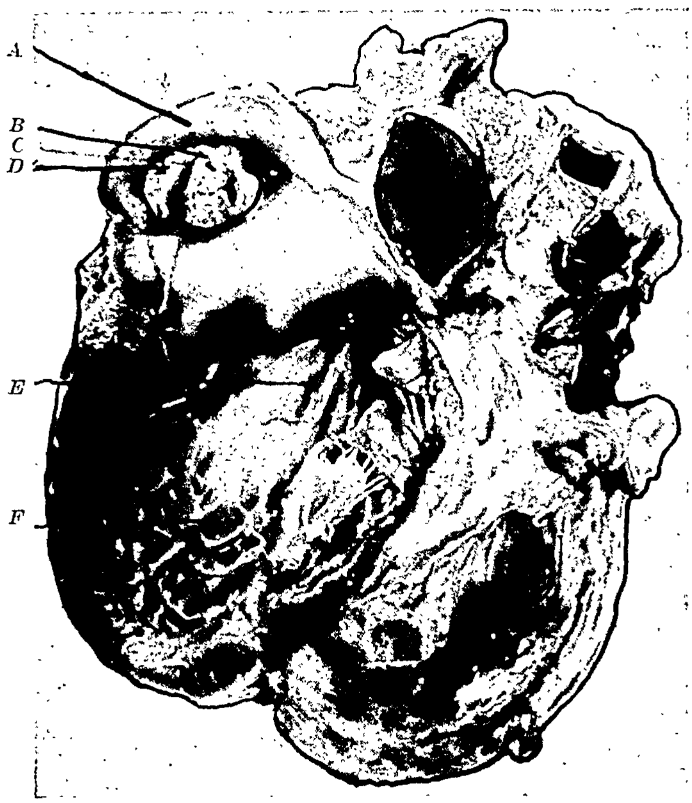

Fig. 1.—View looking down on pulmonary valves. *A*, pulmonary artery, stenosed (opened, showing intimal surface); *B*, orifice of pulmonary valve (8 mm. × 2 mm.); *C*, long granular vegetations in umbrella fashion; *D*, pulmonary valves joined at raphe borders; *E*, mitral valve leaflet; *F*, left ventricle, opened.

noticed at this time that her spleen and liver had become greatly enlarged. No record was kept of her temperature.

On September 11, the following physical examination was made after she arrived in New York:

Positive Findings.—The mucous membranes were pale and a small petechia was observed in the right conjunctiva. The spleen was hard, firm and greatly increased in size, reaching almost to the umbilicus. The liver was about two fingers below the costal margin. The cardiac examination was the same as had previously been observed. It was noticed at this time that she was running a temperature, varying between 100° and 104°.

Laboratory Findings.—Blood cultures, September 13 and 15. No growth. Blood count: red blood cells, 3,950,000; white blood cells, 6,500; hemoglobin 60 per cent; urine, many red blood cells and a few granular casts.

During the next two and a half months her condition was progressively more septic. There was no clinical evidence of infarction, except that she complained a good deal of cough. Edema of the legs and vulva was noticed, which spread upward to the thighs and back. She complained a good deal about bleeding from her nose, and she had intermittent attacks of bloody diarrhea. On November 13, 1928, a purulent discharge was noticed coming from the vagina. A vaginal examination was made, but there was no evidence of localized abscess. Petechiae in various parts of her body at this time were noted. On November 28, a generalized petechial rash appeared over her entire body, and she became stuporous and irrational. This rash faded somewhat during the following week. On December 2, she died suddenly.

Ante-Mortem Diagnosis.—Chronic cardiac valvular disease; mitral stenosis and insufficiency; cardiac hypertrophy; subacute bacterial endocarditis; infecting organism unknown.

Fig. 2.—Teleroentgenogram of chest.

(Diagnostic note.) On first examination, the notes show that a diagnosis was made of "probable congenital lesion." This was founded primarily upon the following: a loud pulmonary murmur, the history obtained, and the electrocardiogram which was quite characteristic. This diagnosis was never revised. The patient drifted into the group of mitral cases, and the original classification was more or less in the background.

Summary of Autopsy Performed on December 2, 1928, at a Private Undertaker's Establishment.—Heart. The pericardium is slightly bulging. The contents consist of about 40 c.c. of fibrinous, flaky serum. The visceral and parietal layers show a shaggy hair-like exudate. There are a few easily broken-down adhesions about the basal portions. The heart weighs 280 gm. and is greatly enlarged in its right chambers, the apex being formed by the right ventricle, the left not appearing on the anterior aspect. A striking feature of the organ is the marked dilatation of the right auricle and the distinct hypertrophy of its wall, the columnae carneae being held out in bold relief. A small foramen ovale is closed. In the posterior auricular wall, just about the orifice of the coronary sinus, are two saccular, pocket-like adhesions, with a rounded muscular fence with muscular

puckerings. The valve at the orifice of the coronary sinus is lengthened, measuring 1 cm. The tricuspid orifice in circumference is 9.6 cm. The cusps are moderately but evenly thickened. There are slight nodular thickenings just behind the free margin of the cusps at the attachment of the chordae tendinea but the chords themselves are neither thickened nor shortened. There are a few firm, warty, calcific nodules, 4 cm. in diameter on the auricular surface of the leaflet. The right ventricle is astonishingly hypertrophied, the wall measuring 2 cm. in thickness through the region of the conus arteriosus. The papillary muscles, particularly the pectinate muscles, are very prominent and enlarged. The musculature of the

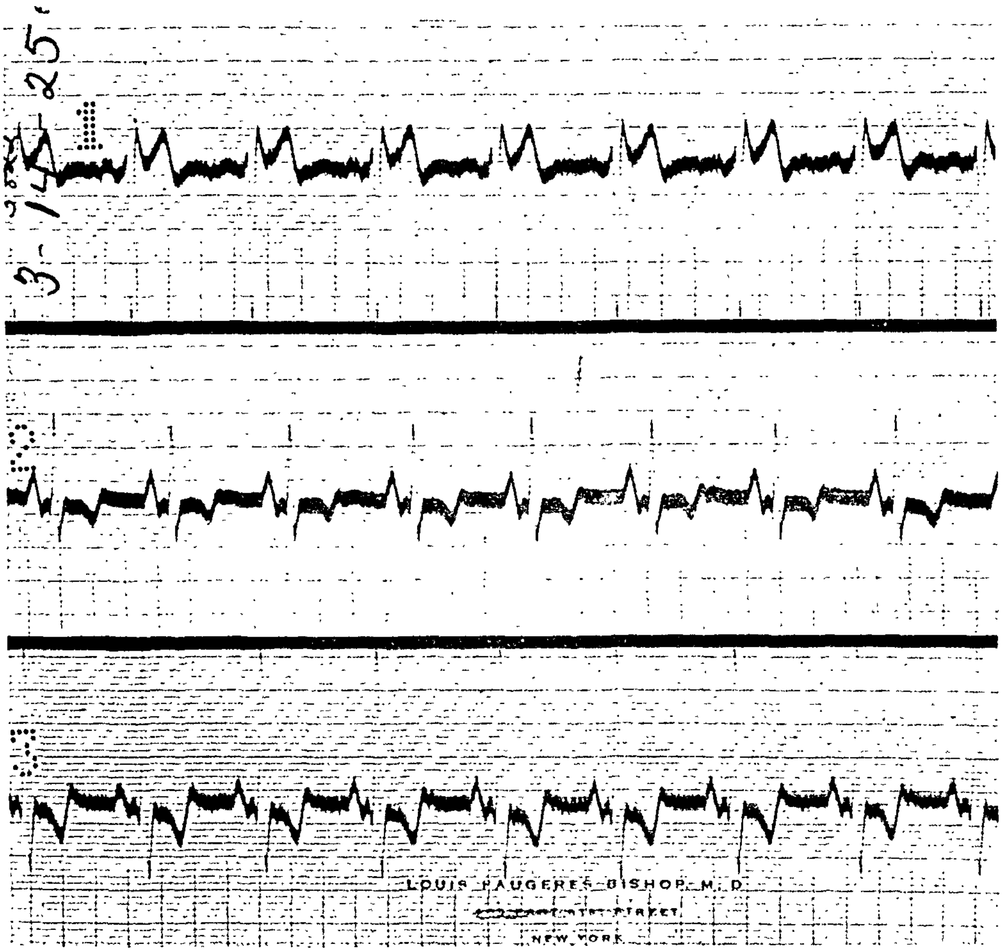

Fig. 3.—Electrocardiogram showing marked right ventricular preponderance characteristic of congenital heart disease, and inverted T-wave in Leads II and III.

conus arteriosus is particularly hypertrophied, having short longitudinal folds. The circumference of the conus is 4 cm. in its midportions. The endocardium of the entire right ventricle is thickened, opaque and white. The pulmonary orifice measures at the bases of the pulmonary valves 3.75 cm. in diameter. The pulmonary artery is thin-walled. The pulmonary cusps are firm along the contiguous borders, with symmetrical edges, leaving a slit-like orifice 8 mm. long and 2 mm. wide. There is a small raphe showing the attachment of the cusps to each other Across the rim of the valve is a tapering growth of long, granular, greyish vegetations, forming a torn umbrella-like structure. One of these growths is particularly long and tenuous.

The left ventricle appears normal. The walls of the attachment of the posterior

mitral leaflet measure 1 cm. in thickness. Section of the myocardium shows it to be fine and smooth, but irregularly interrupted by pearly grey, diffuse, irregular areas of fibrous change. The mitral orifice is 9 cm. in diameter, the leaflet is entirely normal. The aortic orifice at the base of the semilunar valve measures 5 cm. The aortic cusps are normal in shape but show a line of calcification around the lunulae. The intima of the aorta is smooth and elastic.

The lungs are congested posteriorly. There are a few small, round, raised lumpy patches in the posterior parts of the posterior lobes. Scattered throughout are irregularly bordered dark red areas of partially consolidated tissue with no pleural involvement. The spleen weighs about 900 gm. and has normal general configuration. No congenital notches are observed. Seen through the capsule the organ is a dense purple red color, firm and elastic. On section it is firm, cuts easily, and is of dark red color. Many splenic follicles are seen but no infarcts. The liver weighs approximately 2000 gm. and has a typical "nutmeg" appearance, very dense and firm. The kidney is normal in size and configuration, and of a smooth, dark purple color. Dense, mucous, dot-like areas are scattered throughout the surface and interior of the cortex. On section these are found to be confined to the zone glomeruli.

Microscopical Examination.—Lungs: lobular pneumonia; no infarcts. Liver: advanced chronic passive congestion. Kidney: glomerular nephritis. Spleen: chronic passive congestion. Heart: fibrinous pericarditis with slight reaction in subserous layers; few leucocytes; areas of wide fibrosis in the myocardium; no Aschoff bodies; coronary arteries show no sclerosis.

COMMENT

On account of the fact that cases of pulmonary stenosis reaching adult life, without other congenital heart disease, are relatively rare, we believe they should be recorded. This case is of special interest because the patient lived to adult life and then died as the result of bacterial endocarditis. The infecting organism was not identified.

NOTE.—Unfortunately, due to the fact that this autopsy was done at some disadvantage we did not remove enough of the aorta to include the ductus arteriosus. We have had a personal communication from Dr. Maud Abbott, concerning this case, who tells us that it is very probable that the ductus arteriosus was closed.

Department of Reviews and Abstracts

Selected Abstracts

Burwell, C. Sidney, Smith, W. C., and Neighbors, DeWitt: The Output of the Heart in Thyrotoxicosis With Report of a Case of Thyrotoxicosis Combined With Pernicious Anemia. Am. J. M. Sc. 178: 157, 1929.

A case of thyrotoxicosis complicated by pernicious anemia is reported. The increased demand for oxygen combined with the decreased oxygen carrying power of the blood was met by a great increase in the cardiac output per minute and hence in the work of the heart. Repeated observation of the cardiac output in this case and in a second case of thyrotoxicosis revealed that the adjustment of the circulation to increased demand for oxygen took place by an increase in cardiac output rather than by an increased utilization of the arterial oxygen. When the metabolic rate was highest and the hemoglobin lowest, the cardiac output was approximately 20 liters per minute, an amount ordinarily associated only with severe and short lasting muscular exertion: Following the administration of iodin, the basal metabolic rate, pulse rate and cardiac output all fell while the body weight increased. The question of the effect of digitalis in thyrotoxicosis is not cleared in any degree by these observations.

Schwartze, E. W., Hann, R. M., and Keenan, G. L.: Ouabaine, Physiological Standard for Digitalis, Strophanthus and Squill. J. Pharm. and Exper. Therap. 36: 481, 1929.

As a result of the investigations herein reported, the suggestion was made that in the Revision of the U. S. Pharmacopeia the form of official Ouabaine be changed from that crystallized from water and containing 20 per cent moisture to that crystallized from alcohol to which a little ether has been added and containing approximately 12.5 per cent moisture. This suggestion was adopted by the Committee.

Gröss, Louis, Loewe, Leo, and Eliosoph, Bingam: Attempts to Reproduce Rheumatic Fever in Animals. J. Exp. Med. 50: 41, 1929.

Experiments are described in which an attempt is made to reproduce in animals the lesions characteristic of rheumatic fever in the human. A large number of animals representing 7 species was employed. Among other materials streptococci isolated in pure culture from the blood of rheumatic patients as well as whole blood, plasma, serum, pericardial, pleura and hydrocele fluid, filtrate from tonsils, subcutaneous nodules, lymph nodes and nasopharyngeal washings obtained from such patients were used in a variety of combinations and with a number of procedures calculated to predispose the animal to the disease.

The criteria are given, the fulfilment of which is essential for the establishment of the experimental production of rheumatic disease in animals. These criteria are the reproduction of (1) the Aschoff body, (2) nonbacterial pericarditis (3) nonbacterial verrucous endocarditis. Judged by these criteria, the authors have failed to reproduce the disease and they believe this is true of all the work thus far reported in the literature.

Saphir, Otto: Involvement of Medium-Sized Arteries Associated With Syphilitic Aortitis. Am. J. Path. 5: 397, 1929.

The present study was undertaken as a search for initial or early stages of syphilis in types of vessels whose structures closely resemble that of the aorta. Fifty cases which at autopsy showed grossly and histologically syphilitic lesions in the aorta were used. The innominate artery showed syphilitic changes in 33, the carotid in 29, the superior mesenteric in 10, the inferior mesenteric in 3, the common iliac in 10 and the femoral artery in 7 cases. The subcutaneous artery was examined in 29 cases, 15 of which showed syphilitic lesions.

The syphilitic lesions were characterized by endarteritis of the vaso vasorum and perivascular infiltration of lymphocytes in the adventitia. The media of the elastic type of artery showed an interruption of the continuity of the elastic fibers and fibrotic areas combined with circumscribed lymphocytic infiltration. The media of the muscular type of arteries only rarely showed changes. In the intima circumscribed button-like areas of fibrosis without degenerative changes were found very frequently. These are not specific but are chronic inflammatory in nature and might be associated with any type of pathological lesion in the adventitia.

Paisseau, G., and Oumansky, V.: Intermediary Forms Between Rheumatic Endocarditis and Malignant Endocarditis. Arch. d. mal. du coeur. 22: 652, 1929.

Rheumatic endocarditis produces valvular sclerosing lesions and the results after long years are mechanical, with insufficiency and final failure. Malignant endocarditis which is most commonly grafted on old valvular lesions is essentially an infectious disease with a fatal prognosis showing septicemic manifestations, e.g., anemia, emboli, purpura and Osler's nodes, while the cardiovascular symptoms are less prominent.

In rheumatic endocarditis no causative organism has been proved, while in malignant endocarditis one constantly finds the streptococcus of Schottmüller. This latter though grown with difficulty on the usual media has two characteristics: It is only slightly hemolytic, and it is not pathogenic for animals, though typical lesions can be produced if the valves are first traumatized or if the virulence is raised by repeated transfer. However, there seem to be varieties of endocarditis intermediary in form which have characteristics of both types. Cases of rheumatic endocarditis have been noted which instead of terminating in the usual way with cicatrization show themselves capable of developing the characteristic cardiac changes but without the articular symptoms.

The author quotes Clawson's beliefs on the identity of the organisms of malignant endocarditis and rheumatic endocarditis and the ease of culture of organisms in the latter condition by his own method.

The author believes that those bacteriological findings are in accord with the clinical picture of the disease.

Rheumatic endocarditis is usually accompanied by signs of cardiac insufficiency. There is an absence of splenic enlargement of emboli, and the disease responds to salicylate therapy. On the other hand, in endocarditis lenta the opposite holds, and there are no pleural or pericardial manifestations. However, the value of none of these individual signs is absolute. Salicylates frequently have no effect on the cardiac lesions of rheumatism. Forms of malignant endocarditis exist where cardiac failure does occur and evidences of infection are often slight. Infectious emboli have been observed in rheumatic endocarditis, and Bambonneix has also noted the presence of Raffin-Osler nodes.

The author quotes four cases which support his belief. The first two were sisters from a family of eight. Three had had attacks of acute articular rheumatism and

one of erythema nodosum with articular symptoms. One of the rheumatic subjects died with symptoms resembling infectious endocarditis. Of the other two rheumatic patients, the eldest after history of articular rheumatism developed classical malignant endocarditis of which she died. Embolism of the lungs, kidneys, and spleen was present; the anemia was intense; blood cultures were negative. Autopsy, however, showed no vegetative endocarditis, very little scarring of valves with a large clot partly organized in the left auricle. The younger sister during an attack of acute articular rheumatism suffered numerous bouts of severe purpura. Exophthalmic goiter also developed which was apparently incidental. In this case the purpura and anemia made one think of malignant endocarditis. The consistently negative blood cultures placed it in the class of recurrent rheumatic endocarditis.

Two other examples are cited where purpura was a prominent symptom and where the case did not respond to salicylates. The first, a boy fifteen years old, was a member of a family where three others had suffered from rheumatic heart disease. Purpura and a severe aortic lesion were the outstanding lesions. The second case, a girl twenty-four years old, was seen in her third attack of acute articular rheumatism. Blood cultures were negative, but a purpuric eruption appeared which became spreading and ecchymotic. This became generalized and lasted one month. A pericardial rub was present and an interlobar pleurisy, both of which resolved.

Both cases showed purpura as an outstanding feature. This symptom, though it occurs, is rare in rheumatic heart disease and especially in acute articular rheumatism.

All four cases showed characteristics common to rheumatism and malignant endocarditis. It is possible that in the evolution of the disease a stage is reached which it is impossible to classify as either disease. Diagnosis then rests on autopsy findings or on the recovery of the patient.

Agostoni, G.: A Case of Right Bundle Branch Block Suspected Clinically, Diagnosed With the Electrocardiogram and Proved by Autopsy. Arch. d. mal. du coeur. 22: 577, 1929.

The case observed was that of a man aged twenty-six years, complaining of palpitation and dyspnea on effort. His previous history was not important. The general appearance was good excepting for slight cyanosis of the lips and some dyspnea. Examination of the circulation showed a rapid pulse with occasional extrasystoles. Blood pressure was 100/70-80. A triple rhythm was present especially over the ensiform and due to reduplication of the first sound. At the base the second sound was accentuated over the pulmonary area where there was also a short, soft, diastolic murmur. Orthodiagram showed enlargement of the entire heart with enlargement of the pulmonary hilus. The jugular veins were distended, the liver was enlarged, and slight edema of the lower extremities was present. Wassermann was negative and only a trace of albumin was present in the urine. Triple rhythm without the characteristics of gallop rhythm lead the authors to consider a branch lesion. The electrocardiogram confirmed this. The R-S interval was prolonged. The R-wave being upright in Lead I, inverted in Lead III with the T-wave oppositely directed. Splintering of R I was also noted.

The diagnosis of this lesion was based on a greatly enlarged heart without particular shape, the absence of valvular lesions, the presence of arterial hypotension. Radioscopically the chief points were those of "danse hilaire," that is movement of the hilus shadows with the cardiac contractions. On this sign and the presence of diastolic basal murmur a diagnosis of functional pulmonary insufficiency was based.

At autopsy, it was found that the heart was very big, with the myocardium showing greyish white streaks on section; the endocardium was normal, the pulmonary artery dilated. Histologically the right branch was interrupted in different areas by cicatricial tissue.

The etiology was presumed infectious and possibly of rheumatic origin.

Reid, William D., and Kenway, Florence L.: Electrocardiographic Signs Associated With Low Basal Metabolism. Endocrinology 13: 191, 1929.

No electrocardiographic findings characteristic of low basal metabolism were found in a study of 260 low basal metabolic cases, 260 normal basal metabolic cases and 70 high basal metabolic cases. The changes usually described as occurring in such cases were not found frequently enough to be characteristic. In five untreated cases of myxedema all showed low T-waves, and 4 showed low P-waves as well. R-waves less than 0.5 millivolts were found in three cases, and in each of the remaining two the R-wave equaled 1 millivolt.

Bowers, L. G.: Pericardiotomy for Pyopericardium. Arch. Surg. 19: 301, 1929.

Report is made of a boy aged seventeen years with purulent pericarditis associated with empyema, the result of a left-sided lobar pneumonia. A large amount of pus was aspirated from the pericardium, cultures from which showed pneumococci. Pericardiotomy was performed four weeks after the onset of the acute illness. There was immediate relief, though the patient died one week after the operation with sepsis. The autopsy showed a left empyema, pneumococcus type; complete atelectasis and unresolved pneumonia of the left lung; fibrinopurulent pericarditis; organizing right-sided adhesive pleuritis. A special operative procedure used on the patient is described and presented with the hope that it will stimulate other trials. The author believes that pericardiotomy is a simple operation presenting little or no risk and is capable of saving life.

Two factors are in operation which constitute a serious handicap to the heart's work: first, the degenerative effects in the myocardium produced by the local inflammatory process; second, the mechanical handicap produced by the rapidly increased imprisoned exudate within the sac.

Simon, H.: Plethysmographic Studies of Rhythmic Changes in Vessel Size. Ztschr. f. Kreislaufforsch. 15: 448, 1929.

Studying the spontaneous variations in the volume curve of a rabbit's ear, Simon finds that under similar conditions both ears show the same type of rhythmic change. When the experiment is prolonged and the animals are not kept sufficiently warm, these variations gradually diminish together with a diminution in the total ear volume. In this state, the contracted ear vessels fail to respond to skin stimuli. However, by warming the animal, these rhythmic changes are again brought forth, and the vessels again assume their reflex excitability.

The rhythmic changes disappear after section of the cervical sympathetic, including the stellate ganglion. This procedure causes marked increase in the ear volume on the ipsolateral side.

When one ear alone is warmed from 47° to 50°, the other ear shows a marked increase in total volume, without the appearance of rhythmic changes, however.

When the carotid blood supply was cut off temporarily, a postanemic hyperemia was observed only in normal ears, not in denervated ears.

Schwentker, Francis F., and Noel, William W.: The Circulatory Failure of Diphtheria. Bull. Johns Hopkins Hosp. 45: 276, 1929.

In an analysis of 1600 consecutive cases of diphtheria admitted to the Sydenham Hospital from 1920 to 1927, there were 178 deaths. Of these, 139 followed laryngeal diphtheria while the remaining 39 were definite clinical cases of circulatory failure. According to the clinical course and the findings at autopsy, the authors believe that the evidence allows a classification of circulatory failure of diphtheria into two groups, early and late. This classification is based not on the time of onset of failure but on the appearance of the patient. The cases of early circulatory failure are an essential part of the diphtheria intoxication and are the end-stage of the disease, the result of a virulent infection and too often of neglect on the part of the parents to summon a physician until the condition has become alarming. Vasomotor collapse with toxemia forms the outstanding picture.

Cases of late circulatory failure occurred as early as the eighth day of the disease but usually ten to twenty days after the onset. The usual course was that after a week or more of apparent convalescence, the patient suddenly complained of symptoms referable to the heart. There were disturbances of cardiac rhythm with evidence of congestive failure; death was often very sudden. Thus late circulatory failure is a complication of the disease caused probably by local inflammatory reactions incident to regeneration and repair in the cardiac tissue.

Oettinger, Jacob: Electrocardiographic Changes After Acute Coronary Occlusion. Ztschr. f. klin. med. 110: 578, 1929.

In two cases of acute coronary thrombosis, one of which was confirmed by autopsy, the author found the following electrocardiographic changes:

1. In one case, during the first few days following the occlusion, there was an abnormal elevation of the R-T interval above the base line, the T-wave rising directly from the upper half of the descending limb of the R-wave and merging into the next P-wave. On the sixth day after the occlusion, Lead I showed a sharp inversion of the T-wave.

2. In the second case, low amplitude of the ventricular complex was found with similar changes in the R-T interval.

A note is made of a case of mitral stenosis in which an antemortem diagnosis of coronary embolism, established by electrocardiographic studies, was confirmed by autopsy. This case will be reported elsewhere.

Due credit is given to American workers for their early recognition of coronary thrombosis as a clinical entity.

Jones, H. Wallace, and Roberts, R. E.: The Electrical Axis of the Heart as an Indicator of Changes in Ventricular Predominance. Quart. J. Med. 23: 67, 1929.

The authors have studied the effect of ventricular preponderance on the form of the electrocardiogram in several groups of cases. In order to give a mathematical value to different degrees of preponderance, the calculation of the electrical axis of the heart has been determined by the formula and graphic method proposed by Carter, Richter and Greene. The first group of cases studied showed the effect of respiration and posture on the electrical axis of normal hearts. The group showed that these two factors usually produced profound changes in the position of the heart and form of the electrocardiogram.

In cases where there is a fixed apex beat clinically, due to adherent pericardium, the movements of the electrical axis with respiration show by contrast with the

normal cases no marked difference. Instead of the rotation in direction of the axis with deep inspiration and expiration, there is only an extremely small movement, a *striking result* which provides a valuable test for this lesion. In this group of cases, the authors feel that the change in the electrocardiogram which took place following shift in position of the patient from the right and left side was small.

Cases in which there is complete transposition of the viscera show with the electrocardiogram marked evidence of right-sided preponderance. When the respiratory movements of this group are examined, they are found to be similar to those found in normal individuals except that rotation is in the opposite direction. A recognition of this right-sided preponderance in the first few weeks of life and its return to normal at the end of three months in healthy children is of importance in the early recognition of congenital cardiac disease by persistence beyond the normal period of evidence indicating right-sided preponderance.

In a group of 17 cases with changes in ventricular preponderance with alteration in the cardiac rhythm, the authors found that no change in preponderance took place with the change in rhythm in 10 cases, while the remaining 7, with one exception, showed more evidence of right-sided predominance when the heart was fibrillating than when it was beating with a normal rhythm.

Hughes, F. W. Terrell, and Perry, C. Bruce: Senile Arterial Changes in a Child Aged Seven Weeks. Bristol Med. Chir. J. 46: 219, 1929.

A child, aged seven weeks, suddenly died following a short period of cyanosis and distressed breathing. Post-mortem examination showed a heart normal in size but with marked thickening and tortuosity of the coronary arteries which stood out from the rest of the heart like cords. The valves were normal. On microscopical examination, the coronary arteries showed more or less obliteration by extreme intimal thickening composed of a loosely arranged fibrillar connective tissue. The media was almost completely calcified and only very broken fragments of muscle fibers were left. This change was confined to the larger branches of both coronary arteries, the smaller arteries being normal. Scattered throughout the myocardium were areas of early fibrosis replacing the muscle fibers.

The family history and previous history of the child showed no etiological condition. Wassermann on the mother's blood was negative.

Holt, Evelyn: Chronic Adhesive Pericarditis in Childhood. Am. J. M. Sc. 178: 615, 1929.

The present study is an attempt to follow over as long a period as possible 51 children who have had acute pericarditis or in whom a tentative diagnosis of adherent pericardium has been made. In 39 of the cases there is a definite record of some pericardial involvement, 22 cases are still under observation, 21 have died with 5 autopsies, and 8 have been lost. A detailed analysis of the individual cases follows.

A summary of the clinical course indicates that rheumatic infection occurred in a large number of the children, usually in children at an early age, and was characterized by repeated acute attacks. In 26 of the cases an attack of pericarditis seemed to be a definite turning point, the beginning of a train of unfavorable signs and symptoms, which became progressively worse and usually led to death within a short time. Of the 21 who died all had symptoms and signs of cardiac insufficiency, and in practically every case the apparent cause of death was cardiac failure. The cases showed evidence of continued cardiac infection and progressive damage. The ascites present in 12 patients was associated with cardiac decompensation, and the picture was that of cardiac failure rather than cirrhosis or pseudo-

cirrhosis of the liver (Pick's disease). Auricular fibrillation was observed in 6 of the children. In 4 cases it appeared as part of a general breakdown preceding death. Bacterial endocarditis was present in only 2 of the cases.

The main physical signs associated with adherent pericarditis are described. It is pointed out that adherent pericardium is one form of heart disease most likely to come to the autopsy table undiagnosed. The history of acute pericarditis, the marked increased size of the heart out of proportion to the supposed endocardial or myocardial damage, systolic retraction of the interspaces along the chest wall, fixation of the heart in its position, interference with respiration, dilated veins over the chest wall, occasional pulsus paradoxus are all discussed. Pericarditis is associated with valvular disease usually with mitral stenosis and often with aortic insufficiency.

Clawson, B. J.: The Aschoff Nodule. Arch. Path. 8: 664, 1929.

In this extensive review, the author has attempted to correlate the description of Aschoff bodies as given by different observers and to compare their observations with the material in 50 cases from his own group. He discusses the significance of such a structure in the diagnosis of acute rheumatic fever and concludes that it is doubtful whether the Aschoff nodule should definitely be considered a specific lesion resulting from a specific rheumatic virus. The theories on which the formation of the Aschoff nodule may be formed are discussed.

Nabarro, David, and MacDonald, R. A.: Bacteriology of the Tonsils in Relation to Rheumatism in Children. Brit. M. J., October 26, 758, 1929.

A bacteriological study has been made of the tonsils removed from 50 rheumatic and 48 nonrheumatic children. The streptococci recovered from the tonsils were studied quantitatively and qualitatively as to their various characteristics. No material difference was found to occur between the organisms recovered from the two groups of children. The authors believe that this absence of difference fits in with the theory that there is no specific streptococcus which is the cause of rheumatism but that the condition is due to a hypersensitiveness resulting from repeated small doses of toxin.

In spite of the lack of difference, tonsillectomy in rheumatic cases is probably a valuable prophylactic and therapeutic measure.

McClenahan, W. U., and Paul, J. R.: A Review of the Pleural and Pulmonary Lesions in Twenty-Eight Fatal Cases of Active Rheumatic Fever. Arch. Path. 8: 595, 1929.

The material in this study is based on 28 fatal cases of acute rheumatic fever showing signs of activity in the myocardium or endocardium. Active pericarditis was present at autopsy in 75 per cent and active pleurisy in 64 per cent of the cases. Pleurisy apparently is a specific manifestation of the rheumatic infection and is characterized by the nonsuppurative character of the exudate and absence of bacteria. This lesion resembles the rheumatic pericarditis. It is, as a rule, less extensive than pericarditis and associated with far less serious consequences. It manifests itself in a number of different forms but is generally accompanied by the accumulation of pleural fluid which may be hemorrhagic particularly in young children and is nearly always rich in fibrin. It bears a close resemblance to tuberculous lesions of the pleura but differs from this last infection in that it does not reveal a thickened hyalinized pleura as an end-stage.

There was noted also a definite tendency for the pleurisy to involve the neighboring area of the lungs producing a subpleural pneumonitis.

The authors have also studied the lesions that occur in and about the pulmonary vessels and have found in these patients that there are many arterial changes. They have noted particularly in the cases occurring in childhood the presence of focal or hemorrhagic lobular pneumonia exhibiting certain atypical features. These features differ from ordinary terminal lobular pneumonia. While not specific manifestations of rheumatic fever, these lesions seem to occur fairly commonly in the disease.

Cecil, Russell L., Nicholls, Edith E., and Stainsby, Wendell J.: Bacteriology of the *Blood and Joints* in Rheumatic Fever. J. Exper. Med. 50: 617, 1929.

During the spring of 1928, 29 patients with acute rheumatic fever were subjected to blood cultures; 9 or 31 per cent yielded a streptococcus. During the spring of 1929, 31 patients with acute rheumatic fever were studied by blood cultures; 26, or 83.9 per cent yielded a streptococcus. The higher percentage of positive cultures in the later series appears to have been due to improved cultural methods. Of the 35 strains of streptococci recovered from blood cultures, 33 have been classified as Streptococcus viridans, one as a Streptococcus hemolyticus and one a Streptococcus anhemolyticus. In 7 patients with rheumatic fever who were subjected to cultures from affected joints, 5 or 71.4 per cent yielded a Streptococcus viridans. In 3 patients in whom green streptococci were recovered from both blood and joint, agglutination and absorption tests proved the identity of the strains isolated from the two sources.

These findings, the authors feel, make it difficult to escape the conclusion that rheumatic fever is a streptococcal infection, usually of the alpha or viridans type and at least in its acute stage is a bacteremia with streptococci circulating in the blood stream.

The authors suppose that in rheumatic fever the patient's tissues are allergic to streptococci while in infectious endocarditis (subacute bacterial endocarditis), the tissues are immune to these organisms. A state of allergy toward the streptococcus, however, will probably not in itself induce the lesions or joint manifestations of rheumatic fever without the concomitant presence of streptococci.

Dressler, Wilhelm, and Fischer, Robert: Tricuspid Stenosis. Klin. Wchnschr. 8: 1267, 1316, 1929.

In a very complete clinical and pathologic study, with an excellent review of the literature, the authors conclude that tricuspid endocarditis, resulting in stenosis, is a much more frequent lesion than the textbooks would have us believe. Among their endocarditis cases, they found tricuspid stenosis (with insufficiency) in 24 per cent. Pure tricuspid insufficiency is rarer than tricuspid stenosis which is usually combined with insufficiency.

Tricuspid stenosis is usually combined with mitral stenosis and very often also with an aortic lesion. The tricuspid lesion never reaches the severe grade of a mitral stenosis, but the right auricle becomes greatly dilated and hypertrophied. The left auricle is usually not so large as it would be in a pure case of mitral stenosis.

The most frequent cause is acute rheumatic fever, and the female sex suffers predominately.

The most important diagnostic signs are: persistent cyanosis, subicteric tint and liver enlargement, which symptoms persist even after edema and other evidences of decompensation disappear. Of great value is a double-phased liver pulsation with an auricular and ventricular component. This sign is regarded as of much greater significance than the venous pulse. A very constant symptom is a considerable enlargement of the heart to the right side with a regular pulse in spite of a severe

associated mitral stenosis. *By x-ray the heart is found enlarged to the right;* in many cases, there appear no evidence of pulmonary congestion and very little widening of the left auricle.

Tricuspid stenosis definitely adds to the gravity of a pre-existing heart lesion. Nevertheless, compensation may be kept up for years. Thus, Hiller reports a case of a woman fifty-three years old who had 3 attacks of rheumatic fever between nineteen and twenty-nine years. Between twenty-four and thirty-seven, she gave birth to 10 children and continued with her work. After forty-six years of age, she complained of precordial distress but continued to work until eight days before her death.

Adams, Leyland J.: Tuberculosis of the Aorta. Arch. Int. Med. 44: 711, 1929.

The case reported here is one of 33 to be found in the literature where tuberculous lesions have been found in the aorta. The present case is the twentieth instance of tuberculosis reaching the aorta by extension from a tuberculous process outside the aorta.

In this case, the autopsy showed that the involvement extended to the media but that no rupture had occurred. Acute miliary tuberculosis was not present. The lesion had extended from an extensive acute tuberculous involvement of the left pleura.

Clinically, syphilitic aortitis was suspected on account of the history, shortness of breath, pain, pallor and the positive Wassermann reaction.

Anderson, Alan R.: Electrocardiographic Studies in Artificial Pneumothorax and Thoracoplasty. Am. Rev. Tuberc. 20: 728, 1929.

Electrocardiograms made on 100 consecutive admissions to a tuberculosis sanitorium have shown very little deviation from the normal. Electrocardiographic studies were made on 50 patients with artificial pneumothorax and 8 cases with thoracoplasty. Neither the degree of pulmonary collapse maintained nor the duration of the collapse therapy had any definite relationship to the form of the electrocardiogram. Axis deviation of the heart occurred with right pneumothorax in 36 per cent of the cases.

These studies would not indicate that any of the patients were afflicted with a degeneration of the cardiac muscle. The clinical data would appear to bear out this contention.

Goldring, William: Edema in Congestive Heart Failure. Effectiveness of Diuretics as a Guide to Prognosis. Arch. Int. Med. 44: 465, 1929.

In a series of 46 patients with congestive heart failure in whom edema was not relieved by digitalis, diuretics were successful in 25 cases (54 per cent). While cardiac edema can generally be relieved by digitalis and rest in bed in most instances, in those patients in whom digitalis is ineffective diuretics may be produced frequently by drugs belonging to the xanthine group. The author believes that of these drugs theophylline and merbaphen in combination with ammonium chloride have been most useful.

Merbaphen is a double salt of sodiumoxymercuriochlorphenoxy acetate with diethyl barbituric acid, containing about 33.9 per cent of mercury in a complex nonionizable combination employed in a 10 per cent solution. It is best used in combination with ammonium chloride. This drug should be used with precaution when there is an associated nephritis, hypertension, exudate or hemorrhage in the retinas and even in the case of elderly persons.

The greatest incidence of reaction was noted in the rheumatic group with persistant cardiac activity. This observation is in contrast to that made by Marvin in a similar group of patients. The author believes that the cessation of diuretic effect from other drugs before edema is completely relieved is due to a temporary depletion of blood chloride. The diuresis following the use of sodium or ammonium chloride in combination with diuretic drugs indicates that the blood chloride level is raised above the renal threshold.

The failure of reaction to adequate digitalization indicates a marked diminution of cardiac reserve. Even when the patients subsequently reacted to a diuretic by complete relief from edema, length of life exceeded six months in only one of the forty-six patients. This observation compares with those made by Marvin in his group of patients.

Burnett, Clough Turrill, and Piltz, George F.: The Electrocardiogram in the Acute Infections. J. A. M. A. 93: 1120, 1929.

The authors have studied a series of 100 patients who, following some acute infection, were especially studied with reference to possible heart injury. None of these had showed any signs or symptoms of heart disease prior to the recent infection. No cases of scarlet fever, diphtheria or frank rheumatism were included, and none of these patients gave a history of rheumatic fever. Twenty-eight of these furnished significant changes in the electrocardiogram. The changes consisted of prolongation of the P-R interval to or beyond 0.20; inversion of the T-wave in one or more leads; slurring or bizarre R-waves or low voltage in more than one lead, premature beats and sinus block. In 20 of these patients symptoms and other signs of heart disease were lacking or confusing and in only 3 of the 28 were either heart signs or symptoms sufficient to indicate heart injury.

While the occurrence of these changes in the electrocardiogram may or may not indicate pathological changes in the heart, the authors regard them as significant.

They believe that pathological and clinical evidence supports the view that in the course of many types of acute infection, the heart tissues are injured. The electrocardiogram offers a means of diagnosis in a sufficiently large proportion of these cases to render its more general employment worth while.

Book Reviews

APPLIED ELECTROCARDIOGRAPHY. By Aaron E. Parsonnet and Albert S. Heiman. New York, 1929, The Macmillan Company.

The material of this book is divided into three main sections. The first of 51 pages is devoted to a discussion of the physiological basis of electrocardiography, the electrocardiograph, its description and technic. The latter subject is presented in considerable detail since many of the minor points about conducting a "heart station" are described. While such descriptions may seem superfluous to advanced readers, the points taken up are essential to those beginning the subject and would prove invaluable on such occasions. The second section of 130 pages is devoted to a discussion of the various disorders of the heart, disturbances of the conducting system, diseases of the ventricle and disturbances of coronary circulation. These subjects are presented in the usual manner with electrocardiograms illustrative of each phase of the condition. One hundred and twenty illustrations are included in the text. These reproductions of the electrocardiograms are for the most part clear and ample. A discussion of the various conditions included is brief and met in such a way as to be easily understood by those not necessarily familiar with the "trade terminology" of electrocardiography. There is a short section devoted to a schema for electrocardiographic reading. This book should appeal especially to physicians and students desiring a general information about the subject of electrocardiography without too much detail as to variations and theoretical discussions. It is complete, it is brief, it is ample, and it should be useful. The bibliography concludes the volume.

CARDIAC ARRHYTHMIAS; CLINICAL FEATURES AND MECHANISM OF THE IRREGULAR HEART. By Irving R. Roth. New York, 1928, Paul B. Hoeber, Inc.

In an introduction by Dr. E. Libman, the statement is made that the impulse to prepare this volume came as the result of an exhibit made by Dr. Roth at the meeting of the American Medical Association in May, 1925. The exhibit was widely admired and its importance for purposes of instruction so much appreciated that Dr. Roth was urged to publish his diagrams in book form. This he has done in this volume with sufficient text to describe the anatomy and physiology of the heart, the mechanism and clinical characteristics of the various types of arrhythmias.

Eighty illustrations and five tables are included in a text of 205 pages. The first section is devoted to the anatomy and physiology of the heartbeat. The normal electrocardiogram and its manner of production by instrumental means are discussed. In a second section of cardiac arrhythmias there is a discussion with electrocardiograms illustrating each type including sinus arrhythmia, auriculoventricular heartblock, extrasystolic arrhythmias, paroxysmal tachycardia, flutter and fibrillation and combined arrhythmias. The text is well prepared, is amply illustrated by electrocardiograms and diagrams to show theoretically the explanation of the disorder. The text is brief, is well written and is easy to read.

Clinical Aspects of the Electrocardiogram; A Manual for Physicians and Students. By Harold E. B. Pardee. New York, 1928, Ed. 2, Paul B. Hoeber, Inc.

In this volume of 235 pages, the author discusses the normal electrocardiogram and its variations and presents a section on the technic of recording the electrocardiogram and the management of the string galvanometer; then follow in turn the changes due to hypertrophy of the auricles and ventricles to myocardial abnormality and the clinical significance of abnormal waves. A section is devoted to disturbances in rate or rhythm, and under this heading are discussed the various irregularities of the heart. Electrocardiograms illustrative of each disorder are shown by illustration; the nature of the disturbance and its possible explanation are discussed as well as treatment. An important section is devoted to a discussion of the clinical aspects of normal rate and rhythm, especially in regard to diagnosis of these conditions without the aid of instrumental means. This very important chapter should prove valuable to those interested in clinical heart disease. The interpretation and clinical application of the electrocardiogram is presented in detail. There are 60 illustrations showing typical electrocardiograms, figures illustrating explanations of the text and the instruments that are in use in electrocardiography. An extensive bibliography adds greatly to the value of the text.

Clinical Electrocardiograms; Their Interpretation and Significance. By Frederick A. Willius. Philadelphia, 1929, W. B. Saunders Company.

In this volume of 196 pages there are presented all the various types of electrocardiograms found in disturbances of heart mechanism. The subject matter is divided according to the well-recognized types of disturbances of mechanism, and in each type are discussed the various clinical signs, the types of the electrocardiograms produced by the disorder, the nature of the disorder and such treatment as may be

known for its correction. There is included at the end of each section a full bibliography on the subject. There is no discussion of the instruments of technic or the underlying principles of electrocardiography.

The author has collected a large amount of material and has made excellent selections for illustrations of the type to be presented. A discussion on all points of the clinical disorders is full and very broad in its scope. The possible variations and atypical forms are included in the discussion.

The book should serve as an excellent reference volume for clinicians who may find need for interpretation of an electrocardiogram. In addition, it should interest anyone working in electrocardiography.

These four volumes, together with an additional one *Principles and Practice of Electrocardiography*, by Dr. Carl J. Wiggers (AM. HEART J. 5: 127, 1929), represent a response on the part of workers in electrocardiography and heart disease to the demand for text discussion of the value of the use of string galvanometers in recording electrocardiograms and their interpretation in patients in the treatment of heart disease. This indicates that the demand for such books is widespread and exacting. They supplement the small volume, *Clinical Electrocardiography*, by Sir Thomas Lewis, (London, 1928, Shaw and Sons, Ltd.,) which has now reached its fourth edition. These six volumes are prepared in about the same style allowing for such normal variations as would be expected from authors of such different experiences. Each volume should find its way to the library of workers particularly interested in electrocardiography, and the casual reader must pick and choose the one which appeals most to him. They are all satisfactory from the standpoint of accuracy, completeness and neatness of preparation.

Each author expresses definitely the feeling that string galvanometers are now well-known instruments of precision and are of value in the study of disturbances in mechanism and possibly other diseases of the heart. This subject no longer holds a position of special technic and has now taken its place among other useful means of accurate diagnosis and treatment. Out of the study devoted to clinical electrocardiography has come a better understanding of clinical disorders of the heart: how they may be recognized under ordinary conditions without instrumental means, how they can be probably placed in the general scheme of heart disease, and how they may be used in the treatment of a patient. Without such volumes as are included in this review, disorders of the heart would probably still hold the mys-

THE HEART IN MODERN PRACTICE, DIAGNOSIS AND TREATMENT. By William Duncan Reid. Philadelphia and London, Ed. 2, 1929, J. B. Lippincott.

This book according to the preface, is an attempt to summarize for the practitioner our knowledge of the diagnosis and treatment of

cardiac diseases, with emphasis upon the contributions to this field which have been made in recent years by the introduction of graphic methods and by intensive studies in other directions.

In spite of a good many defects it fulfils this purpose fairly well. The chief criticisms of the reviewer are that the material is poorly organized, there is much evidence of carelessness in wording which results in vagueness and often in misleading statements, and the treatment is uneven so that some important subjects are inadequately discussed.

By organization of material the reviewer refers to the arrangement of the material in the discussion of individual conditions or syndromes as well as to the arrangement of the book as a whole. The emphasis placed upon etiology is commendable, but it seems that this object could have been attained with less repetition and confusion and with greater evenness of treatment than the author has achieved by the arrangement which he has adopted.

As examples of careless wording the following sentences may be cited: "The direction of the wave, as mentioned above, is also dependent upon which electrode first received the current" (page 47). "Since the chief action of the drug (digitalis) is to produce therapeutic heart-block, its administration will rarely prove of value save in cases of accelerated rate of supraventricular origin" (page 108). "Angina pectoris is a clinical entity that is absent after death" (page 387).

As an example of unevenness in treatment resulting in inadequate discussion of an important subject, the discussion of congestive cardiac failure on page 354 may be cited. It is limited to a single page. At the bottom of the page the statement is made that the treatment and other details of heart failure are sufficiently considered in other parts of the book. The index refers under heart failure to pages 20, 33, 78, 189, and 93 as well as to page 354. Reference to these pages does not help the reader to gain a comprehensive idea of the subject.

From the standpoint of the practitioner heart failure is, however, the most important subject that the author could discuss, and the consideration of it should not be so scattered as to be not easily accessible.

The reviewer also feels that in the section on the cardiac irregularities and in some measure in other sections the author is weak in the discussion of the physiological fundamentals.

—*F. N. W.*

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Original Communications

THE ELECTROCARDIOGRAM IN CORONARY DISEASE*

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SCLEROSIS of the coronary arteries is a frequent pathological finding especially after the age of fifty. Benson and Hunter[1] call attention to the high incidence of this condition. They found 200 cases of advanced coronary obstruction in 1750 autopsies. A large number of these autopsies were coroner's cases, and this would tend to exaggerate the incidence to a certain extent. Of 339 consecutive autopsies above the age of forty from the Department of Pathology of the University of Minnesota there were twenty-seven cases of coronary disease or an incidence of approximately 8 per cent.

In a previous report[2] an attempt was made to construct a clinical picture of coronary artery disease from an analysis of the clinical data of a series of fatal cases which came to necropsy. It was found that there were variations in the clinical picture presented and four main types were described. (Table I.) Type 1 includes those cases in

TABLE I

CLINICAL TYPES OF CORONARY SCLEROSIS

CLINICAL FEATURES	NO. OF CASES
1. Heart not enlarged, congestive failure absent; symptoms of cardiac insufficiency absent; heart normal in size; blood pressure normal	43 or 37.2 per cent
2. Heart not enlarged, congestive failure present; symptoms of cardiac insufficiency present; heart normal in size; blood pressure normal	3 or 2.6 per cent
3. Cardiac enlargement, congestive failure absent; symptoms of cardiac insufficiency absent; heart enlarged; blood pressure increased	25 or 22.6 per cent
4. Cardiac enlargement, congestive failure present; symptoms of cardiac insufficiency present; heart enlarged; blood pressure usually increased	43 or 39.0 per cent

*From the Department of Medicine, University of Minnesota, Medical Service, General Hospital.

which the heart is normal in size, blood pressure is normal and symptoms and signs of congestive heart failure are absent. Type 2 has the same features as Type 1 except that congestive heart failure is present. Type 3 consists of those cases in which there is cardiac enlargement, usually some increase in arterial pressure with absence of congestive heart failure. Type 4 has the same features as Type 3 with the addition of the signs and symptoms of congestive heart failure. From the analysis of the data in this series it was apparent that clinical features especially characteristic of coronary disease are often absent and that extensive coronary disease may be present and yet escape detection by our usual clinical methods. For instance, in Type 1 there are no signs which indicate the presence of disease in the heart. There is no cardiac enlargement, the blood pressure is normal, there are no auscultatory signs diagnostic of cardiac involvement. Furthermore, the patient presents no evidence of congestive heart failure during life, since at autopsy the liver shows no passive congestion. In this group particularly it is possible for the cardiac damage to be entirely overlooked. We must rely entirely for diagnosis upon the anginal syndrome presented by the patient. If the typical anginal syndrome as described by Heberden in 1768 were always present, few errors in diagnosis would be made in spite of the absence of characteristic signs in the heart. However, the typical picture as usually described is more often absent. For example, in the analysis of our clinical data, radiation to the left arm was found in only 10 per cent of the cases. The pain was almost as frequently localized to the upper abdomen as to the chest. Furthermore, belching, nausea and vomiting were often associated so that a gastro-intestinal condition was closely simulated. Also in about 10 per cent pain was absent, and the attack consisted of an acute respiratory distress resembling bronchial asthma. These atypical subjective features and the paucity of characteristic physical signs make the diagnosis of coronary disease by our simpler clinical methods frequently very difficult.

Experimental and clinical investigations have shown that usually the electrocardiogram is definitely altered by disturbance of the coronary circulation. Studies by Smith[3] on the effect of ligation of the coronary arteries have demonstrated the sequence of changes in the electrocardiogram very clearly. Disturbance in the coronary circulation to the left ventricle in dogs is followed shortly by inversion of the T-wave. Hamburger[4] and his co-workers found similar alterations in the electrocardiogram following experimental coronary embolism by injection of a suspension of lycopodium spores into the coronary circulation. In the literature, electrocardiographic changes associated with clinical cases of coronary disease are frequently mentioned, but detailed reports on series of cases are comparatively few. Pardee[5] in an analysis of fifty cases of coronary sclerosis found the changes that appear in

Table II. Oppenheimer and Rothschild[6] show that coronary disease is the most frequent pathological condition which produces widening and notching of the QRS and alterations of the T-wave. In forty-seven cases with abnormal ventricular complexes, thirty-eight showed coronary disease at autopsy.

TABLE II

HEART DISEASE AND ABNORMAL ELECTROCARDIOGRAMS (PARDEE)

	CORONARY OCCLUSION ACUTE AND CHRONIC
Coronary T-wave	18
Downward T-wave in Lead I or Lead II or both	5
Small excursion of T-wave (low voltage)	0
Notched QRS group	2
Small excursion of QRS (low voltage)	3
Bundle-branch block	6
Normal QRS and T-wave except for R. V. P. or L. V. P.	16
Total	50

TABLE III

ELECTROCARDIOGRAPHIC FINDINGS IN 60 CASES OF CORONARY SCLEROSIS

	NUMBER	PER CENT
Inversion of T-wave	53	88
Lead I	24	40
Leads I and II	9	15
Leads II and III	17	28
Leads I, II and III	3	5
Coronary T-wave (Pardee)	13	21
Changes in QRS		
Bundle-branch block	6	10
Arborization block	2	3.3
Moderate notching	11	18
Slight notching	18	30
Low Voltage	9	15
Prolonged P-R	4	6.6
Arrhythmias		
Extrasystoles	11	18
Auricular fibrillation	4	6.6
Complete heart-block	1	1.6
Ventricular Preponderance		
Definite left	18	30
Slight left	18	30
Slight right	2	3.3

The present report consists of an electrocardiographic study of sixty cases of coronary disease. The diagnosis of coronary disease was made either from autopsy findings or from a characteristic clinical picture and outcome. Only those cases were selected in which the electrocardiogram showed a deviation from the generally accepted normal. This analysis therefore does not attempt to determine the incidence of an abnormal electrocardiogram in coronary disease. There is no

doubt that coronary disease may exist without any definite electrocardiographic abnormality. Pardee's analysis indicates significant changes in about 70 per cent of cases. The present report is concerned with a statistical analysis of the electrocardiographic alterations in those cases of coronary sclerosis in which the electrocardiogram showed some distinct abnormality. Table III is a summary of these findings.

The most frequent electrocardiographic deviation was inversion of the T-wave which was present in 88 per cent of the cases. The possible effect of digitalis was excluded in all cases. This observation agrees with that of Pardee who found T-wave inversion in twenty-three of thirty-four cases in which there was an abnormal electrocardiogram. Willius and Brown[7] noted T-wave inversion in 14 of 17 abnormal electrocardiograms of coronary sclerosis. Smith[3] found that ligation of the ramus descendens or circumflex branch of the left coronary artery in dogs is uniformly followed by inversion of the T-wave. Ligation of the right coronary vessels produces no such change. Apparently this cannot be wholly applied to the human heart. In two of the autopsied cases in this group there was a thrombus occluding the right branch. In one instance, there was inversion of the T-wave in Lead I and in the other in Leads II and III. This may be explained by individual variations of the coronary distribution in the human heart. Pardee[5] has described a peculiar type of T-wave which he considers as specific for coronary disease and which he has designated as the coronary T-wave. The characteristic features are a downward sharply peaked T-wave with an upward convexity of the S-T or R-T interval. In Table II it will be noted that of twenty-three instances of T-wave inversion eighteen showed a coronary type of T-wave. In the present series there were fifty-five cases of definite T-wave inversion with but thirteen showing this type of wave. These observations indicate that although the coronary T-wave of Pardee is frequently associated with coronary disease, ordinary T-wave inversion without any special features is equally significant for the diagnosis of coronary sclerosis. It is not to be concluded that inversion of the T-wave is specific for coronary arterial disease. Experimentally it is possible to produce negativity of the T-wave by other means than by vascular occlusion, such as by cooling the apex of the heart,[3] by introducing certain substances such as digitalis[8] or diphtheria toxin[9] and by stimulation of the vagus nerve.[10] Likewise, clinically, inversion of the T-wave is seen in cases of hypertension in the absence of coronary disease, especially with left ventricular preponderance, and also less frequently in valvular disease. T-wave negativity is also found following severe diphtheria[9] and in myxedema.[12] There is little doubt, however, that it is found with the greatest frequency in coronary disease. The less frequent causes of T-wave inversion can usually be easily

excluded and particularly in the absence of cardiac enlargement and congestive heart failure as occurs in Type 1, T-wave inversion may be considered as practically pathognomonic of coronary sclerosis.

Alterations of the initial portion of the ventricular complex, the QRS, were less frequent than changes in the T-wave. There were six cases showing the features of bundle-branch block; a ventricular complex of diphasic character, high amplitude with widened notched QRS. Five of the electrocardiograms of bundle-branch block were those which are generally accepted as indicating right bundle block. There was one instance of left bundle block. There were two cases of widened, notched QRS of low amplitude, the features as described by Oppenheimer and Rothschild of arborization block. It is generally accepted that aberration of the QRS is an evidence of disturbance in the intraventricular conduction. Although rare cases of transient or intermittent bundle block have been reported,[12] most abnormalities of the QRS of this type are permanent and fixed. This suggests that the pathological condition affecting the architecture of the intraventricular conduction system is a permanent anatomical type such as myocardial fibrosis. Clawson[13] has shown that extensive fibrosis in the ventricles is almost entirely due to coronary disease and also that there is a close relation between the location and extent of the fibrosis and the distribution and degree of coronary sclerosis. It is not surprising therefore to find those abnormalities of the QRS associated with coronary disease.

Of considerable interest is the frequency of lesser degrees of notching of the QRS without increase in the time interval. The correlation of such deviations with pathological change in the heart is less definite, since such changes are found associated with normal hearts, especially in the third lead. However, certain observations indicate that these minor changes in the QRS are much more frequent in cardiac disease. Wedd[14] studied thirty cases showing slight notching of the QRS, and definite cardiac lesions were present in twenty-one. Willius[15] believes that notching and slurring of the QRS in isolated derivations indicate local disorders in the myocardium affecting the conducting system. Pardee[16] states that such aberrations of the QRS can be considered normal only when found in one lead and that lead being of relatively small excursion. If present in two leads it can be considered normal only when the notching occurs near the base line. It is never normal according to Pardee to find notching in three leads or near the peak of the R in a lead of relatively large excursion. Ferguson and O'Connell[17] in an electrocardiographic study of 1812 healthy midshipmen at the Naval Academy found notching of the QRS in about 10 per cent. In every instance it was confined to Lead III. In the present series of cases of coronary disease there were twenty-nine cases showing minor notching of the QRS, an incidence of 48 per cent as

compared with 10 per cent in the above-mentioned normal group. Furthermore, of these twenty-nine cases only five showed the notching limited to Lead III. In the remaining twenty-four cases it was present in the other leads, and in eighteen instances it was present in more than one lead. From these observations it seems justifiable to conclude that minor notching of the QRS, especially if present in Leads I and II, is frequently indicative of pathological changes in the myocardium and should arouse a suspicion of coronary disease.

Electrocardiograms of low voltage were noted in nine cases, or 15 per cent of the series. The records were considered as being of low voltage when the maximum amplitude of the QRS in all leads was less than 5 mm. above or below the base line. There is a difference of opinion concerning the significance of this type of electrocardiogram. Sprague and White[18] analyzed fifty-seven cases, of which thirty-four showed evidence of arterial sclerotic heart disease, ten were diagnosed as myxedema and thirteen classified as miscellaneous. These observers conclude that low voltage is of definite significance as indicative of myocardial involvement. Willius and Killins[19] more recently found 140 records showing these features in the material at the Mayo Clinic, or an incidence of 0.3 per cent. Thirty-two per cent of these cases showed evidence of cardiac disease, the remaining 68 per cent included a variety of conditions not associated with heart disease. These observers do not believe that electrocardiograms of low voltage unassociated with other abnormalities indicate any serious myocardial disease. The observations of Willius and Killins unquestionably show that low amplitude records may be found without cardiac damage. However, as with minor notching of the QRS, the question of relative frequency in cardiac disease as compared with normal is of importance. Willius and Killins in their survey of general material at the Mayo Clinic found an incidence of 0.3 per cent as compared with 15 per cent in our group of coronary disease. The frequency of low voltage in the coronary group was therefore about fifty times that of the series reported by Willius and Killins. It would seem, therefore, that this deviation in spite of its occasional occurrence in the normal cannot be entirely disregarded as an evidence of myocardial involvement.

Prolongation of the P-R interval occurred in but four cases, or 6.6 per cent. Every case of increased P-R interval was associated with an abnormal ventricular complex of bundle-branch block. It is apparent that the junctional tissues are infrequently affected in coronary disease and then only when there is vascular obstruction to the septum so that one of the main branches of the bundle is involved. There was one instance of complete heart-block which also showed auricular fibrillation.

Arrhythmias.—The most frequent irregularity was the extrasystolic type which was present in eleven cases or 18 per cent. Auricular

fibrillation occurred in but four cases or 6.6 per cent. In every instance the auricular fibrillation was associated with signs of congestive failure. It has been a matter of common observation that angina pectoris is very infrequently associated with auricular fibrillation. In the present series there was no case of coronary disease of Type 1 or Type 3, i.e., cases with only the anginal syndrome, which showed auricular fibrillation. The case of complete heart-block with auricular fibrillation has already been mentioned. Paroxysmal tachycardia, especially of the ventricular type, has been noted with coronary disease. Although there were several histories suggesting the presence of such attacks, this arrhythmia was not present in any case at the time of taking the record.

Ventricular Preponderance.—There were thirty-eight cases which could be considered as showing some degree of ventricular preponderance. The bundle-branch group was not considered and was not included. Excluding this group any alteration in the direction and amplitude of the QRS which in any way suggested preponderance curves was included. Eighteen cases, or 30 per cent, showed the features of a definite preponderance, left ventricular in every case. There were eighteen cases showing a slight degree of left preponderance and but two of slight right preponderance. There are undoubtedly two chief reasons for the frequency of left ventricular curves. First, coronary disease is often associated with hypertension and cardiac enlargement of the left ventricular type, and this accounts for most of the definite left preponderance curves. Second, it is well known that the form of the normal electrocardiogram is to a considerable degree dependent on the position of the heart. This has been emphasized by Herrmann and Wilson[20] in their study of ventricular preponderance. The characteristic electrocardiogram of the stout, broad-chested individual with a transversely placed heart shows either a low QRS in Lead III or one which is directed downward to some degree. This undoubtedly explains the majority of slight left preponderance curves since it is in the hypersthenic type that coronary disease most commonly occurs. The frequency of left preponderance curves in contrast to those of right preponderance may have some practical application. On several occasions the following condition has been encountered. In an elderly individual with a previous history of a cough and paroxysmal dyspnea followed by signs of congestive heart failure it is often necessary to differentiate between primary right heart failure and coronary disease with congestive failure. Since most cases of primary right heart failure show a definite right preponderance, coronary disease can be excluded largely on this feature alone.

Following is a group of illustrative cases showing the various types of electrocardiographic changes in coronary disease.

CLINICAL REPORTS

CASE 1.—A. G., male, aged 57 years, suffered from attacks of precordial distress three to four years. He was in the hospital for several months for these attacks and discharged with a diagnosis of hypertension and coronary disease October 24, 1927. Two days later he had a severe attack of precordial pressure lasting several hours. After two days he had another severe attack and was again admitted into the hospital. The blood pressure was 230/130 mm.; there were many moist râles in the lungs. During his stay in the hospital he had many attacks of acute orthopnea lasting up to several hours, when he would sit up gasping for breath, his lungs were filled with high-pitched bronchial râles and many coarse bubbling râles. At times there were intervals of several weeks be-

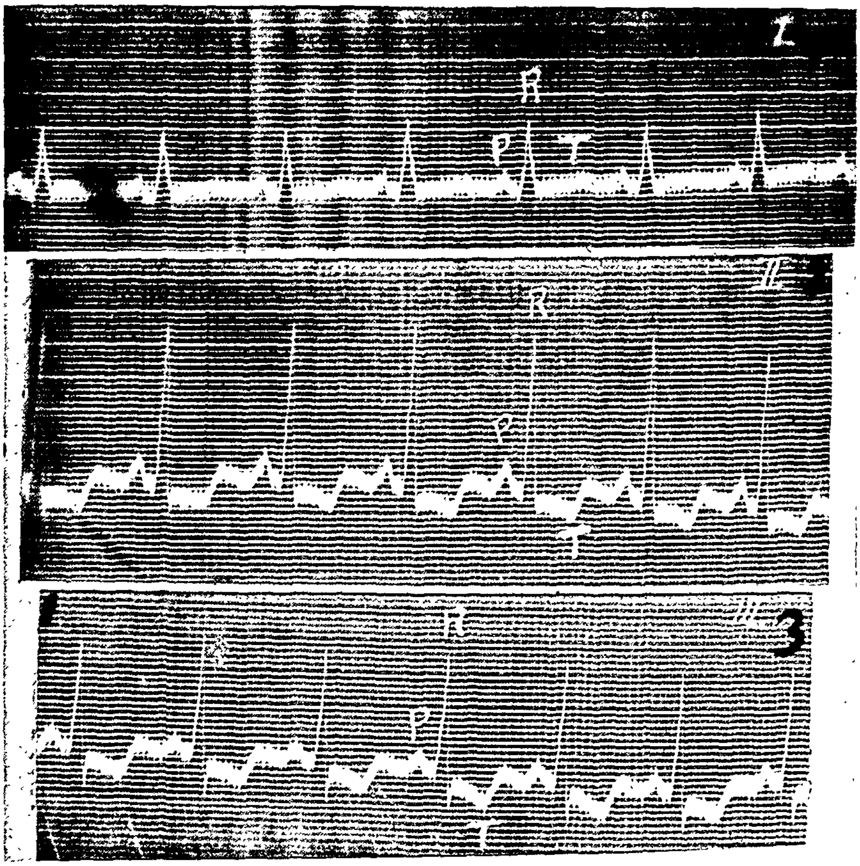


Fig. 1.—Case 1. Leads I, II and III; inversion of the T-wave in Leads II and III. Autopsy showed marked thickening of the small branches of the coronary arteries and areas of fibrosis and necrosis in the myocardium.

tween attacks, at others times they occurred daily. He was in the hospital from October 28, 1927, until he died, May 15, 1928. He had fever for ten days preceding his death and signs suggesting consolidation during the last few days. He apparently died of bronchopneumonia.

At autopsy the pericardial cavity showed 50 c.c. of clear fluid, the heart was enormously enlarged, weighing 990 gm., and there was extreme hypertrophy of the muscle of the left ventricle. There was a large area of scarring with considerable depression in the muscle of the left ventricle. There was very marked thickening of the small branches of the coronary arteries but no actual thrombosis. Microscopically the heart showed marked myocardial fibrosis and some small areas of necrosis with hyalin change. The right lung showed bronchopneumonia. An

electrocardiogram taken October 29 (Fig. 1) showed a definite inversion of the T-wave in Leads II and III with some slurring of the QRS. Repeated electrocardiograms taken during his stay in the hospital showed similar findings.

Case 2.—F. H., male, aged 70 years, admitted to the hospital October 27, 1926, died November 16, 1926. His complaints were pains in the chest, cough, and shortness of breath. He had had a dry cough for ten days. On the day before admission on getting out of bed he had been seized with a severe pain in the anterior chest. During the attack, which lasted about three hours, he perspired a great deal. In the evening the pain returned, and he described it as a pressure being exerted on an area about the size of the fist to the left of the middle sternum. The pain was intense but there was no radiation. He had had no previous attacks of this kind. On examination there was some dyspnea, some cyanosis of the lips, pulse rate was 60, radial arteries were very sclerotic, heart seemed slightly enlarged, heart sounds were distant, there were no murmurs, blood pressure was 125/75 mm. He had an occasional attack of pain while in the hospital but seemed to be getting along very well. He died suddenly, however,

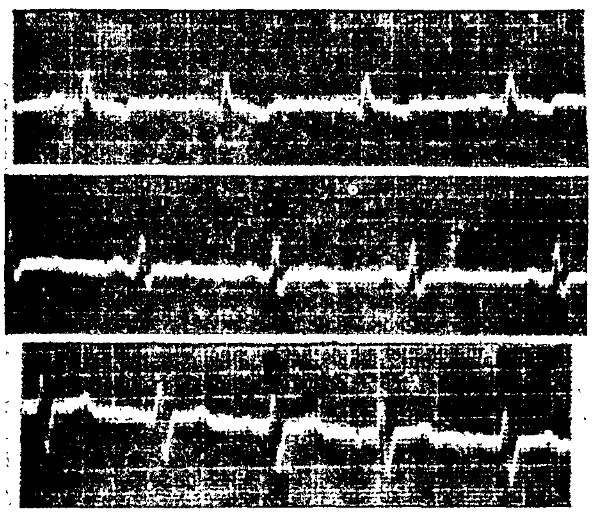


Fig. 2.—Case 2. Leads I, II and III showing inversion of the T-wave in Lead I. Autopsy showed the lumen of the left coronary artery practically obliterated by sclerosis, numerous areas of softening and fibrosis in the heart muscle.

November 17, 1926. Leucocyte count was 14,000, urine was negative. Three electrocardiograms were taken during the stay in the hospital and all showed a definite inversion of the T-wave in Lead I. The first two tracings showed ventricular extrasystoles and some notching of the R in Lead I. At autopsy there was a slight increase of fluid in the pericardial cavity, the heart weighed 540 grams, there were numerous areas of softening in the muscle and fibrosis, the left coronary artery was markedly sclerotic, but it was impossible to demonstrate thrombosis. Lumen of the artery was practically obliterated.

Case 3.—N. R., female, aged 86 years, admitted to the hospital April 15, 1927, died April 22, 1927. She had had attacks of precordial pain and epigastric distress for five years. Her previous health had been good. April 2 she had a severe attack of pain starting in the precordium and radiating to the left shoulder and left side of the neck and left arm. She was holding an infant in her arms at the time and raising it up and down. A physician diagnosed the condition as neuritis. On the morning of admission she had another severe attack of a similar nature. She was then brought to the hospital. On admission her pulse was 84,

extrasystoles were present, the heart sounds were muffled, there were no murmurs, the heart did not appear enlarged to percussion. The blood pressure was 96/60 mm. and leucocyte count 11,300. During her stay in the hospital she had frequent attacks of epigastric and precordial pain requiring the use of morphine. On the day of her death she had a very severe attack, became cyanotic, and died in the attack. At autopsy the visceral and parietal pericardium at the apex of the left ventricle were adherent. Weight of the heart was 400 gm., and there was a widespread softening and thinning of the left ventricle. Just above the apex the softening was so marked that there was almost a rupture of the heart wall. There was a thrombus of the entire descending branch of the left coronary artery, and this artery showed marked sclerosis of its walls. The liver showed some chronic passive congestion. An electrocardiogram showed a definite inversion of the T-wave in Leads I and II with arching of the R-T interval, described as characteristic by Pardee.

Case 4.—O. S., male, aged 64 years, admitted May 10, 1923, in serious condition, died the afternoon of the same day. Patient was seen at his home three days

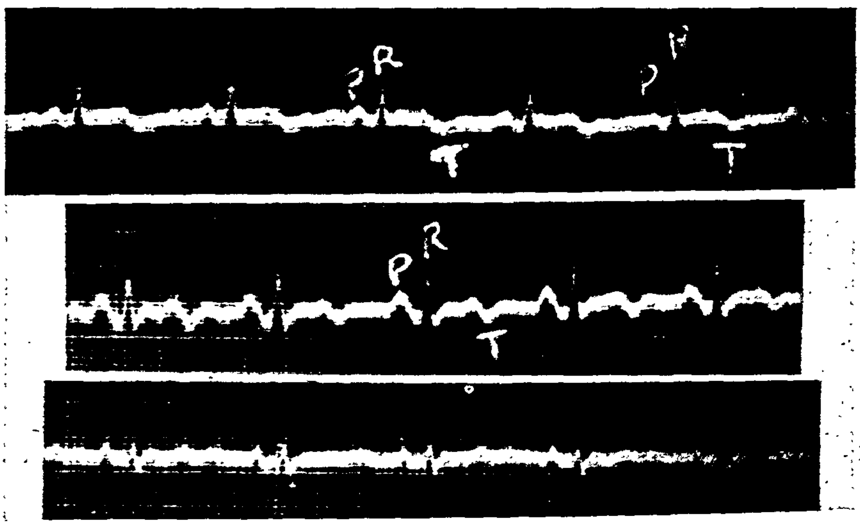


Fig. 3.—Case 3. Leads I, II and III showing inversion of the T-wave in Leads I and II with upward convexity of the R-T portion. (Coronary T-wave of Pardee.) Autopsy findings were sclerosis and thrombosis of the left coronary artery with widespread softening and thinning of the left ventricle.

before admission when he had complained of a constant pain in the left chest and left arm of several days' duration. He had treated it as rheumatism. The pain also radiated to the left side of the neck and the suboccipital region. Except for the pain, the patient appeared to be in good condition and examination of the heart was negative. The day before admission the patient began to vomit persistently, at times the vomitus being dark brown in color. He felt weak and dizzy prior to the vomiting and later became short of breath. His past history was essentially negative. Physical examination showed a well-developed and well-nourished man complaining of severe pain in the chest and vomiting. There was a diffuse slaty cyanosis, no edema, the heart did not appear enlarged. The heart sounds were muffled, pulse was fairly rapid and weak, blood pressure was not obtainable, extremities were cyanotic and cold. The diagnoses considered were ruptured bleeding ulcer, some type of drug poisoning, or coronary disease. Since bleeding ulcer was considered, a transfusion was given. He died two hours after this transfusion. Electrocardiogram showed a deep inversion of the T-wave in Leads II and III. (Fig. 4.) At autopsy there was no edema, there was a general

cyanosis of the entire body, the heart weighed 440 gm., the cavity of the left ventricle was not dilated, but there was a slight increase in the thickness of the wall. The muscle showed no decrease of consistency and on section very little evidence of fibrosis. The left coronary artery showed irregular patches of intimal thickening some of which were calcareous, some of the small muscular branches showed complete occlusion. There was a nondetachable blood clot in the right coronary artery, 3 cm. from its origin. The smaller branches showed changes similar to those in the left coronary artery. There was no apparent softening of the wall in connection with the thrombus. The liver was not congested. The stomach contained about 100 c.c. of dark brown bloody fluid, there was no evidence of ulcer, there was a submucous extravasation of blood in the region of the cardia which suggested this point as a possible source of the hemorrhage. Microscopic examination of the heart showed no evidence of interstitial fibrosis in the sections examined. The thrombus in the right coronary artery showed a laminated structure, many leucocytes, fibrin and hyalinized red blood cells. In this instance there was a marked T-wave inversion with thrombosis of the right coronary artery, but no anatomical change in the region supplied by the artery

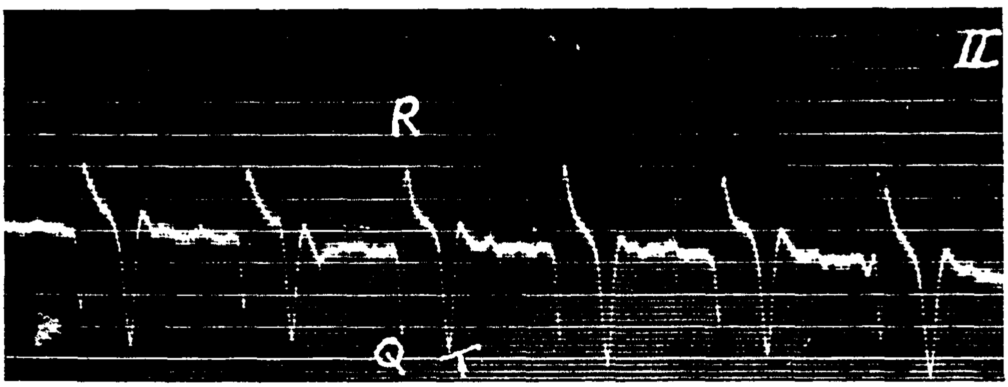


Fig. 4.—Case 4. Lead II showing deep inversion of the T-wave. Autopsy showed sclerosis of smaller branches of both coronaries and a recent thrombus in the right coronary artery 3 cm. from its origin. No softening of the myocardium.

to explain the abnormal electrocardiogram. It is evident that a demonstrable anatomical alteration in the myocardium subsequent to vascular occlusion is not necessary for the production of a high-grade electrocardiographic change.

CASE 5.*—W. H. J., male, aged 69 years. Present illness began in 1921 with painful muscle cramps usually in the legs and side of the chest. Patient stated he had had these attacks during the past seven or eight years. The attacks lasted from three to fifteen minutes and were relieved by rubbing the affected muscle. The blood pressure was 152/90 mm. In October, 1925, while walking uphill he had a sudden feeling of constriction in his chest. Since that time he has had similar attacks on exertion. In November, 1925, he had a severe attack while delivering a sermon. This was relieved by nitroglycerine. Since February, 1926, he suffered from dyspnea and orthopnea at night which was relieved by nitroglycerine. Blood pressure was 128/80 mm. In July, 1926, he still complained of these nocturnal attacks, his heart showed no murmurs. In August, 1926, blood pressure was 130/80 mm. In January, 1927, he contracted an acute respiratory infection. On examination he showed some left ventricular enlargement, no murmurs, blood pressure 120/80 mm. There were some moist râles at the lung bases

*I am indebted to Dr. T. A. Peppard for the opportunity of including Cases 5 and 8.

and some edema of the lower extremities. An electrocardiogram (Fig. 5) showed the features of a right bundle-branch block. An x-ray October 15, 1925, showed MR 5, ML 10.5, total chest width 30.3 cm.

The patient was in the hospital from February to June, 1927, with signs of congestive heart failure and responded very slowly to treatment but finally improved so that he was discharged on May 25, 1927. On September 9 he again complained of attacks of asthma-like dyspnea and was very edematous. Attacks of dyspnea were relieved by ephedrin. He developed a marked oliguria and died October 16 with an anuria of two and one-half days' duration.

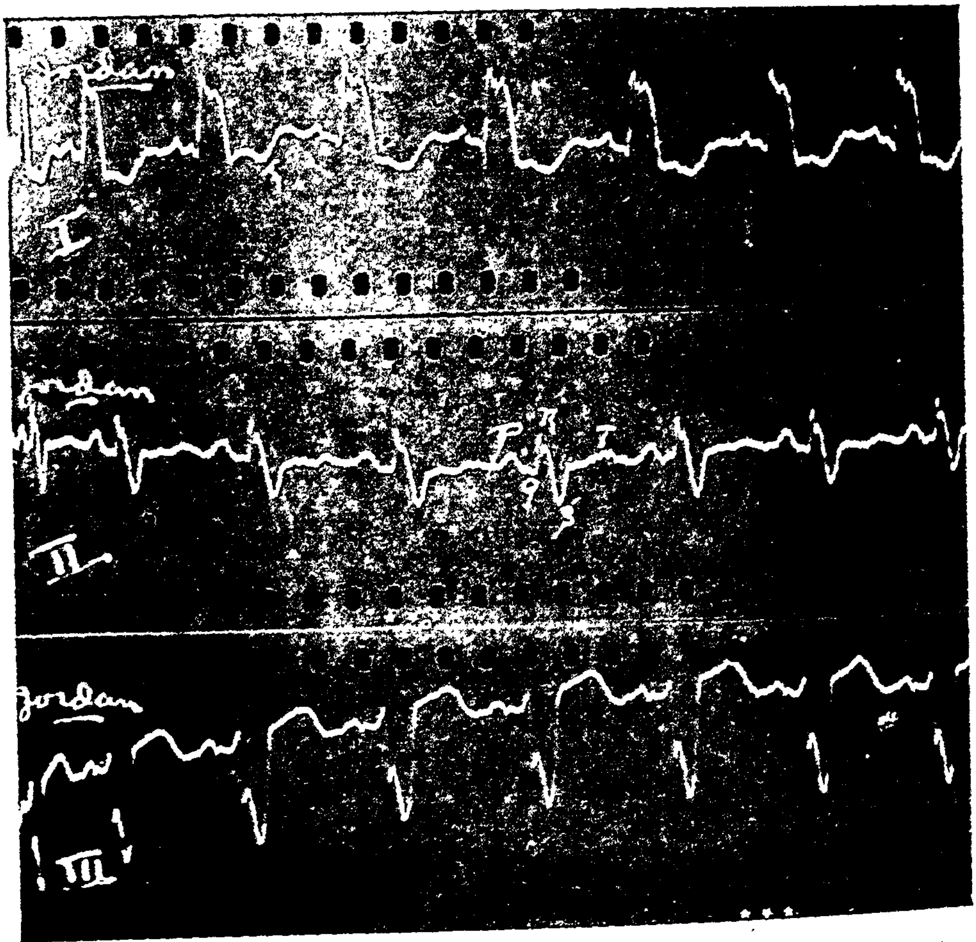


Fig. 5.—Case 5. Leads I, II and III showing right bundle-branch block. Autopsy showed extensive coronary sclerosis especially of the left coronary with almost complete closure of the anterior descending branch; lower half of the anterior part of the left ventricle markedly thinned and replaced by scar tissue.

At autopsy there was considerable edema of the extremities, the heart weighed 600 gm., there was marked hypertrophy of the left ventricle and to some degree of the right ventricle also. There was no disease of any of the valves. There was marked sclerosis of the coronary arteries, especially of the left, with almost complete closure of the anterior descending muscular branch of the left coronary. A large part of the lower half of the anterior wall of the left ventricle was markedly thin, its thickness being less than half that of the other part of the ventricle. The thin part showed a large amount of scar tissue, and on the endocardial surface there was a massive thrombus covering the entire area. The root of the aorta showed a few elevated calcified nodules on the aortic wall. The

liver showed definite passive congestion, the kidneys grossly were quite negative and on microscopic section showed only a moderate arteriosclerosis.

CASE 6.—C. H., female, aged 56 years, admitted April 25, 1927, died June 26, 1927. Patient complained of a heavy feeling in the stomach with pressure as if choking for three months, attacks of shortness of breath for the same duration. The patient had known she had diabetes for one and one-half years and had had the anginal symptoms for three months. The attacks occurred on exercise, but at times wakened her at night so that it was necessary for her to sit up to breathe. Her diabetes had been mild and insulin unnecessary. Physical examination showed a very obese woman in no particular distress. Her heart was enlarged, of the hypertension type, auricular fibrillation was present. There were no murmurs. Blood pressure was 170/100 mm., the liver was definitely enlarged, and there was a mild edema of the ankles. Electrocardiogram showed auricular fibrillation with low voltage in the first two leads with distinct notching of the QRS without widening, and depressed T-waves. The urine showed no sugar. After

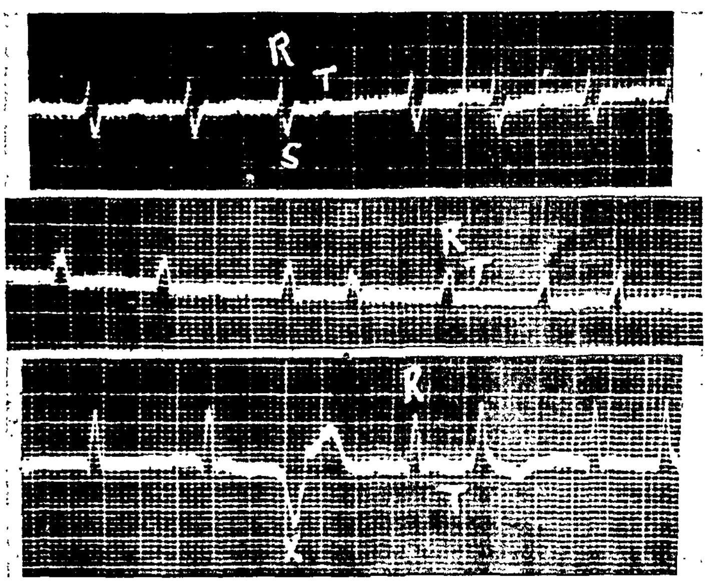


Fig. 6.—Case 6. Leads I, II and III. Auricular fibrillation and only slight alterations in the ventricular complex, slurring of the QRS in Leads I and II. Autopsy showed extreme sclerosis and thrombosis of the right coronary artery and widespread scarring of the myocardium.

a temporary improvement she gradually became weaker until her death on June 26. At autopsy the lungs showed a moderate congestion; the heart weighed 460 gm.; there was extreme sclerosis and thrombosis of the right coronary artery; the left coronary vessel showed only a moderate sclerosis; the myocardium exhibited widespread scarring, there was no definite softening. This is an example of coronary disease with widespread myocardial damage showing only minor electrocardiographic changes, a definite slurring and notching of the QRS.

CASE 7.—C. F., male, aged 66 years, admitted January 25, 1924, died February 17, 1924. Two years before the patient had a sudden pain in the chest and feeling of constriction and suffocation, pain radiating to both arms. In the past few months the patient had been wakened often at night by attacks of shortness of breath. Recently he had dizzy attacks on sudden movements such as turning his head or getting out of bed. On examination he showed some dyspnea, râles at the lung bases and many wheezy bronchial râles. There was moderate edema of

the ankles. An electrocardiogram (Fig. 7) showed low voltage in all leads, with the T-wave in the first lead leaving the R definitely above the base line. On February 17 he had an attack which was apparently a cerebral accident. His right arm and left leg became flaccid; he was unable to talk, became irrational and died four hours after the onset. At autopsy the heart weighed 420 gm. The pericardial cavity contained about 100 c.c. of slightly cloudy fluid and a few fibrin flakes. There was a mural thrombus at the apex of the left ventricle, and the myocardium at this point showed much fibrosis. The main coronary branches showed extensive sclerosis, and at one point in the left coronary the lumen was about 80 per cent occluded. The liver showed some congestion. In this instance there was extensive coronary disease, especially on the left side, showing only low voltage and changes in the R-T interval in the first lead.

CASE 8.—T. S. S., male, aged 55 years. Ten years before he had been told by a life insurance examiner that he had high blood pressure, but he had no symptoms at that time. The present illness began three years ago. After walking four or five blocks he experienced a pain in the back between the scapulae. If he continued walking, the pain would extend down both arms. If he rested, the

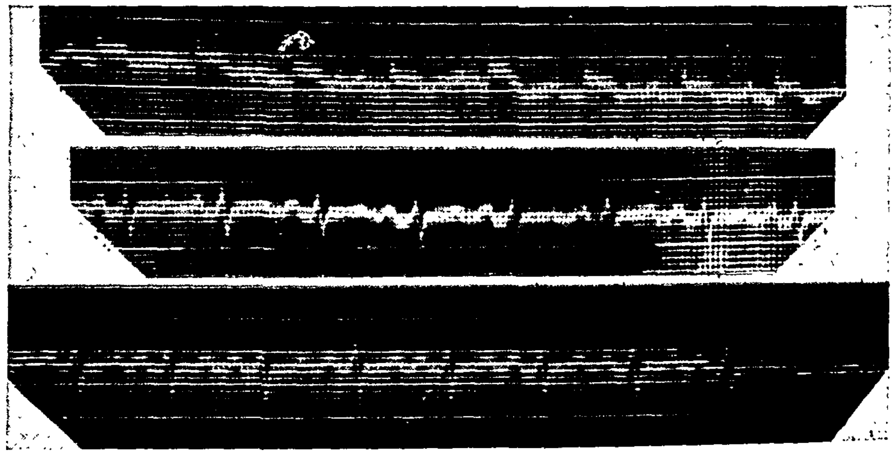


Fig. 7.—Case 7. Leads I, II and III showing only low voltage and T_1 leaving the R above the base line. Autopsy findings were extensive coronary sclerosis with the left branch almost completely occluded at some points, also marked fibrosis at the apex of the left ventricle.

pain disappeared but frequently recurred on further effort. At times he noticed that the pain would develop as soon as he began playing golf, but if he continued it would pass off. The attacks occurred on excitement as well as on exertion. The pain always localized to the middle of the back and when severe radiated to both arms. There was never any pain in chest or epigastrium. He noticed a little shortness of breath during the attacks. An electrocardiogram (Fig. 8) showed depression of the T-wave in Lead II, inversion in Lead III and slight slurring of the QRS in all leads. He developed a very severe attack while he was making an after-dinner talk twelve days before his death. Two days later a pericardial friction rub was heard. At this time he showed a temperature of 101° and a leucocytosis of 13,000, and pericardial friction was heard for two days. An x-ray film showed definite left ventricular enlargement; no murmurs were heard. Systolic blood pressure was 180 three years before, and one year before it was the same. January 7, 1926, during a severe attack systolic pressure was 138. On January 17, 1926, the patient developed a sudden attack of dyspnea while lying in bed, became unconscious and died within a few minutes.

Autopsy showed a heart weighing 550 gm. The visceral pericardium was

slightly roughened on the lower half of the right ventricle, but there was no exudate. There was a marked hypertrophy of the left ventricle with only moderate dilatation; there was no disease of any of the valves. The left coronary artery showed extreme calcification so that it had a bony hardness. The lumen was narrowed and practically occluded in several places in the descending branch to the left ventricle and in the auriculoventricular branch. Occasional small thrombotic masses were found in the narrowed lumen. There was extensive infarction of

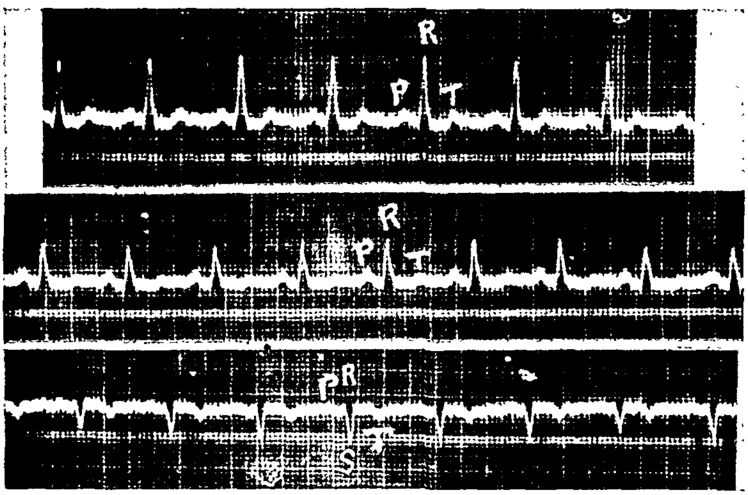


Fig. 8.—Case 8. Leads I, II and III showing only slight slurring of the QRS at the apex in all leads, depressed T-wave in Lead II and inverted T-wave in Lead III. Autopsy showed extreme sclerosis of the left coronary with marked narrowing of the lumen and extensive myocardial softening.

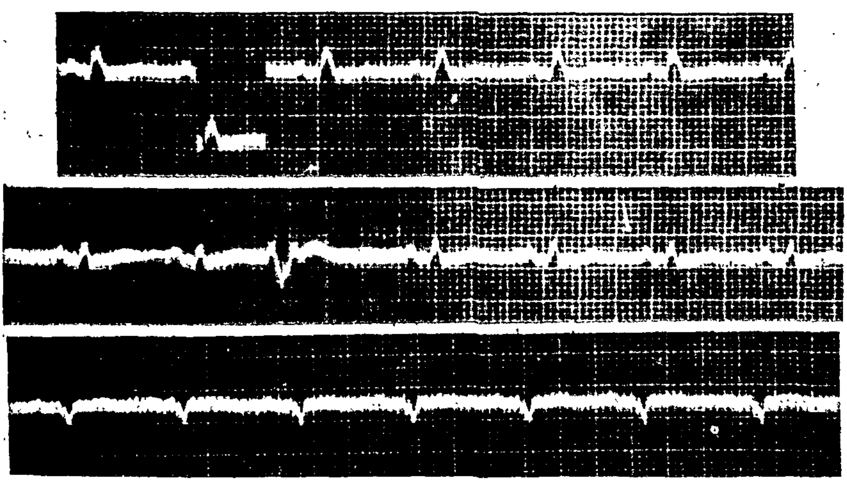


Fig. 9.—Case 9. Leads I, II and III showing very low voltage and slurring of the QRS in all leads. Autopsy showed a very severe degree of coronary sclerosis especially of the left with almost complete occlusion of the circumflex and main descending branches; myocardial fibrosis most marked at the apex.

the interventricular septum and of the lower half of the left ventricle, especially anteriorly. The myocardium in these portions was opaque and softened. There were small areas of softening in the upper half of the lower ventricle. The right coronary artery showed marked thickening of the wall and some narrowing of the lumen, but the lumen was not occluded at any point. The root of the aorta showed only occasional small yellow patches. There was a marked congestion of the liver. The pathological diagnosis was marked coronary sclerosis

with coronary thrombosis and infarction. This case illustrates extensively coronary disease with minor electrocardiographic changes.

CASE 9.—J. C., male, aged 70 years, admitted first to the General Hospital in 1928 because of pain in the extremities, swelling of the ankles, attacks of precordial pain. It was found that the patient was suffering from a definite diabetes. There was a large amount of sugar in the urine at times and blood sugar was elevated. The heart was moderately enlarged, tones distant, and blood pressure was 108/46 mm. An electrocardiogram (Fig. 9) showed low voltage with definite slurring of the QRS in all leads. He was discharged after two months in the hospital. He was readmitted in January, 1929, with dyspnea and edema. The blood sugar was 0.28 per cent, which dropped to normal on treatment and the urine became free of sugar. After eighty-one days in the hospital he was discharged very much improved. His last admission was on April 29, 1929, when he showed signs of advanced cardiac decompensation with generalized edema. The heart was enlarged to the left, there was enlargement of the liver. An electrocardiogram on this admission showed the same features as on the previous admission. On June 3 he developed an erythematous area on the face suggesting erysipelas and was transferred to the contagious ward. On the following day he suddenly became

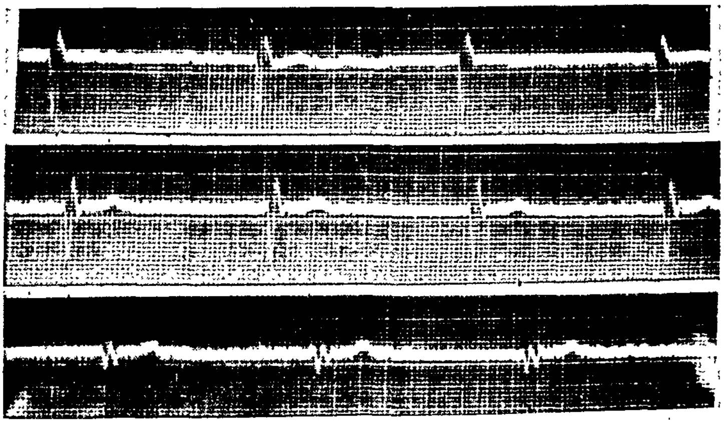


Fig. 10.—Case 10. Leads I, II and III showing auricular fibrillation and complete heart-block, also some widening of the QRS. Autopsy findings were advanced sclerosis of the left coronary artery and its branches.

cyanotic and died. At autopsy a generalized edema was present, and fluid in the abdomen. The heart weighed 400 gm., and the left ventricle was definitely dilated but showed very *little hypertrophy*. *A very severe degree* of coronary sclerosis was present, most marked on the left. The first portion of the circumflex branch to the left ventricle was almost completely closed. The main descending branch was also markedly calcified and the lumen so narrowed that in portions only a capillary opening remained, the right coronary artery was only moderately involved. The septal portion of the myocardium was quite free of fibrosis, but in the apex fibrosis was very marked and there was a definite thinning of the wall. In the wall of the right ventricle there was only one small area of fibrosis. The liver showed passive congestion, and there was a generalized arteriosclerosis present. In this case there was extensive coronary disease, especially of the left side, with definite fibrosis in the myocardium exhibiting an electrocardiogram with only minor changes, low voltage and notching of the QRS in all leads.

CASE 10.—A S., male, aged 74 years, admitted March 18, 1927, died April 27, 1927. On the day before admission he suddenly fell, striking on the left side of the head. He was not unconscious but the fall was followed by a definite left-

sided hemiplegia with difficulty in speech. Previous history was not important with the exception that he had shortness of breath on exertion for the past seven years. On examination the patient was dyspneic, with Cheyne-Stokes respiration, a left hemiplegia was present, blood pressure was 230/70 mm., radial pulse 36, there were extrasystoles present. The heart seemed definitely enlarged to the left, and there was a soft systolic murmur at the apex. The patient seemed to improve as far as the paralysis was concerned but the dyspnea and orthopnea continued, and the blood pressure remained high. On the morning of the day before his death he became unconscious, and the nurse reported that he had a convulsion preceding this. The pulse could not be felt, faint heart sounds could be made out 10-12 times a minute, which would suddenly change to 44 per minute. He was given artificial respiration and was conscious by evening but had convulsive movements of both arms and legs. On the following morning he had a similar attack. On this occasion the pulse could not be felt and no heart sounds were heard. He was given 2 c.c. of adrenalin into the heart and in a few seconds the heart began to beat at a rate of 120 up to 132. It seemed totally irregular. It remained rapid for ten minutes and then suddenly stopped. He was given another injection of adrenalin but there was no response.

Two electrocardiograms were taken (Fig. 10) during his stay in the hospital. Both showed a ventricular rate of 40 with regular rhythm. The P-wave was absent, and the diastolic period showed the typical irregular oscillations of auricular fibrillation. The electrocardiogram, therefore, showed auricular fibrillation with complete auriculoventricular dissociation. The duration of QRS was increased to from 0.14 to 0.16 of a second. There was some slurring in Leads I and II and a definite notching in Lead III. The downward QRS in the first lead gives the tracing the features which are suggestive of left bundle-branch block. At autopsy the pericardial cavity was widely dilated, the heart weighed 705 gm., and there was an advanced sclerosis of the left coronary artery and its branches. Examination of the region of the bundle of His showed no fibrosis grossly. There was very little fibrosis throughout the myocardium. Microscopic examination of the bundle of His showed some change consisting of vacuolization and thinning of the fibers. The liver showed evidence of chronic passive congestion.

CLINICAL MATERIAL

A detailed analysis of the clinical data is not included in this report. In ten cases the clinical features were those which are considered as characteristic for an acute coronary occlusion by a thrombus. This diagnosis was confirmed by autopsy in four instances. The remaining fifty cases presented the picture of chronic narrowing of the coronary vessels. Of the sixty cases, twenty-five could be classified as belonging to Type 1 following the classification of Table I. This group differs from the other types of coronary disease in that definite cardiac enlargement, hypertension, and congestive heart failure are absent. As mentioned previously, this type of coronary disease often presents considerable difficulty in diagnosis. Analysis of the electrocardiographic findings of these twenty-five cases reveals no essential differences from the remainder of the series. There were two instances of right bundle block and one of low voltage. In the remaining records the significant alteration was in the T-wave. From pathological studies the similarity of electrocardiographic findings in the various types of coronary scle-

rosis is to be expected, since the intensity of the sclerotic change bears no relationship to the presence or absence of cardiac enlargement or of congestive heart failure. Coronary sclerosis and myocardial fibrosis is present in hearts of normal size, associated with normal livers, with the same degree of severity as in enlarged hearts with livers showing passive congestion.

POST-MORTEM MATERIAL

Sixteen cases came to autopsy, all showing extensive coronary disease. No attempt will be made in this report to correlate the extent and site of the anatomical change with the form of the electrocardiogram. Of these sixteen cases, eleven presented the more marked changes

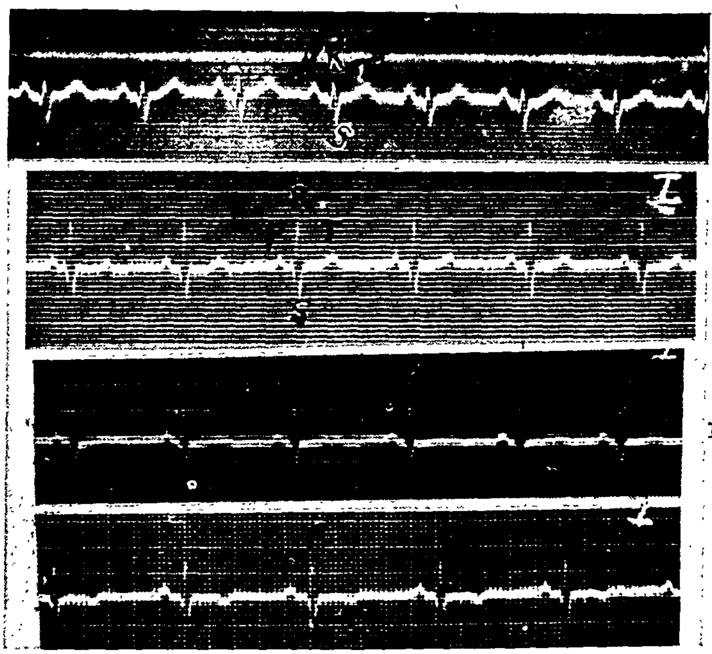


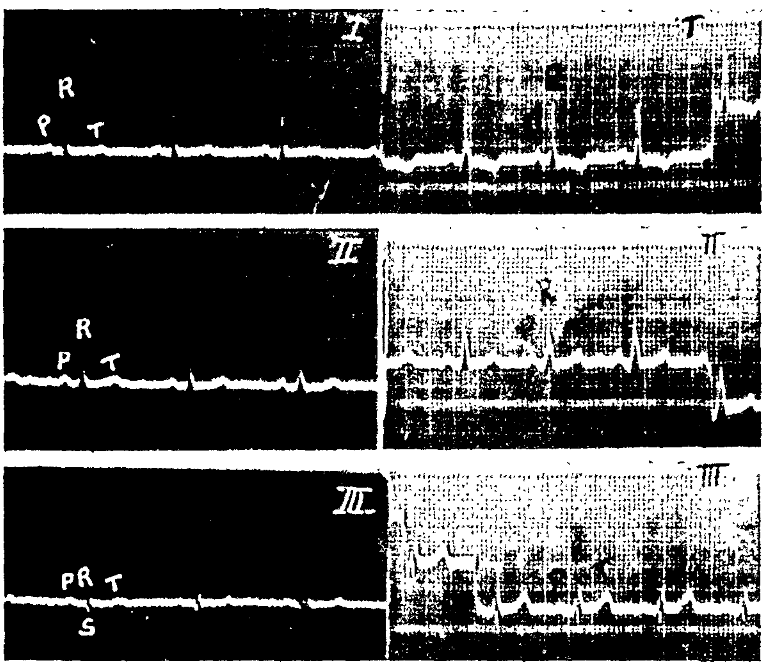
Fig. 11.—Lead I showing changes in the T-wave with depression and finally inversion after a period of three and one-half years. Anginal attacks began in 1924 but became more frequent and severe in 1927.

mentioned, definite aberrations of the QRS and inversion of the T-wave. In five cases the minor electrocardiographic alterations were present such as low voltage, lesser degrees of slurring and notching of the QRS or depression of the T-wave without inversion. Cases 6, 7, 8 and 9 are illustrative of extensive coronary disease showing the lesser degrees of abnormality in the electrocardiogram.

PRACTICAL APPLICATIONS

In the application of electrocardiography to the diagnosis of coronary disease, the following conception seems justifiable. The presence of T-wave inversion in significant leads or widened, notched QRS of bundle-branch or arborization block definitely indicates myocardial dis-

ease which, with some exceptions, is associated with coronary sclerosis. The chief exceptions, hypertension heart with a large dilated left ventricle, aortic valvular disease, the postdiphtheritic heart and myxedema heart, can be easily differentiated and excluded. In the absence of any symptoms or signs indicative of these conditions, as is especially true in Type 1 of coronary disease, the above-mentioned electrocardiographic changes can be considered as definitely diagnostic of coronary sclerosis. The lesser deviations of the electrocardiogram, low voltage, minor notchings and depressed T-wave, while not pathognomonic of coronary disease should not be disregarded. When the clinical picture is suggestive, the presence of these lesser changes should be con-



A. B.

Fig. 12.—(*A*). Leads I, II and III three months after the onset of typical anginal attacks. (*B*). T-wave in Lead I definitely inverted six months later.

sidered as additional support for the diagnosis of coronary disease. Especially in cases of depressed T-wave subsequent observation may reveal the development of a definite inversion (Figs. 11 and 12).

SUMMARY

From an analysis of the electrocardiographic findings in sixty cases of coronary sclerosis, T-wave inversion was found to be the most common abnormality, occurring in 88 per cent of the cases. Widened notched QRS was present in 13.3 per cent.

Attention is called to certain less definite changes such as minor notching of the QRS without widening and also low voltage. An attempt is made to evaluate the significance of these changes.

Increase in auriculoventricular conduction time was comparatively rare and found only associated with curves of bundle-branch block.

The most frequent arrhythmia was the extrasystolic type, which was present in 18 per cent. Auricular fibrillation was present in only 6.6 per cent and only in those cases showing evidence of congestive heart failure.

Preponderance curves of left ventricular type of definite or slight degree were noted in 60 per cent and slight right preponderance in only 3.3 per cent.

The presence or absence of cardiac enlargement or congestive heart failure seems to have little effect on the type of electrocardiogram.

A conception as to the practical application of electrocardiography in the diagnosis of coronary disease is suggested.

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THE CARDIAC RESPONSE IN ACUTE DIFFUSE GLOMERULONEPHRITIS*

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UNTIL recently, attention has been directed, almost exclusively, to the renal phases of acute diffuse glomerulonephritis. It has now, however, become generally recognized that simultaneously with the onset of acute glomerulitis there occurs a sudden rise in blood pressure. Despite the fact that this premise is well established, little attention seems to have been given to the symptoms which follow in its train. The importance and significance of the circulatory phenomena which usher in an attack of acute diffuse glomerulonephritis have not, in the writer's opinion, been sufficiently appreciated.

During the course of study of a series of cases of acute diffuse glomerulonephritis, with reference to the hypertension, it was noted that an unusual number of patients, though they presented unimportant renal symptoms, suffered from a circulatory disturbance. They were not always aware of any discomfort, the information being elicited by direct questions. It was also possible to suspect the presence of acute diffuse glomerulonephritis by a consideration of the mode of onset and the character of the circulatory decompensation, the diagnosis later being corroborated by the presence of hematuria, or urea retention in the blood.

The hypertension in this type of nephritis may be transient, lasting only a few hours. In the majority of cases, however, it persists for days or even weeks, depending upon the severity of the renal disease. Simultaneously with the advent of hypertension, circulatory symptoms appear. There may be dyspnea on exertion, so slight that it can scarcely be noticed by the patient. At times there is definite orthopnea which may cause but little subjective discomfort. In the recumbent position a definite increase in respirations may be observed; also a slight cyanosis around the lips. When told to sit up in bed, these patients acknowledge a sense of relief, previously not having recognized the cause of their discomfort.

In a second group of cases the circulatory symptoms are much more pronounced. The dyspnea is recognized by the patient as a "shortness of breath"; the orthopnea is more distressing, and he is aware of abdominal discomfort. Examination of the abdomen reveals an enlarged liver, often exceedingly tender. Coughing is a common symptom in this type of case. Crepitant and subcrepitant râles, often accompanied by sibilant breathing, are heard throughout the chest. This, with the

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presence of elevated temperature suggests a pulmonary basis for the trouble, but the true condition is finally revealed by a frank hematuria or some other characteristic symptom of acute nephritis.

In a third group of cases the cardiac symptoms predominate. Loud systolic murmurs are heard at the apex, often transmitted into the axilla; murmurs are also heard over the precordium. If the blood pressure has not been noted, or if the hypertension is transient, the basic pathological lesion may be overlooked, particularly if other renal symptoms are absent. On one occasion the writer saw a child, ten years old, with pulmonary edema and anuria, in whom the true cause of the trouble had not previously been recognized. The high blood urea nitrogen in this case disclosed the correct diagnosis.

The precipitant hypertension which follows the sudden onset of acute diffuse glomerulonephritis produces an unexpected strain upon the heart. The hypertension formerly was thought to be caused by an exudative inflammation in the glomeruli, which thus offered a mechanical obstruction to the flow of blood through the capillary tuft. Recently Volhard and Fahr have contended that the initial change in the kidney is a spasm of the afferent arterioles, producing anemia of the glomerular tuft, followed by exudative inflammation. Possibly, the arteriolar spasm is not confined to the kidney. This view seems to explain more clearly the sudden onset of hypertension. It is the sudden strain on the heart which causes it to yield. The gradual development of high blood pressure would never meet with such a response.

In the presence of so great a strain, the right chambers of the heart are the first to give way. The initial evidences of trouble are manifested in dilatation of the heart, congestion of the lungs, and a swollen liver. The heart, however, usually recovers promptly and the circulatory symptoms subside. This right sided decompensation may be so transient that often the symptoms are not apparent; usually they persist for days. On the other hand, if the pathological process in the kidney is intensive, the left side of the heart also yields, intensifying the symptoms of dyspnea and orthopnea, and in many instances leading to edema.

That the heart suffers in acute nephritis has not gone unmentioned in the writings of students of the subject. In 1879 Goodhart[1] wrote: "Probably many are quite alive to the occurrence of sudden death from ventricular dilatation in acute nephritis, but it is not taught as one of the things generally known." He reported five cases of acute scarlatinal nephritis, in four of which post-mortem examinations were performed. These showed dilatation of all cavities of the heart. In another case the right cavities only were dilated, and fatty degeneration of the cardiac muscle was observed. He attributed the cardiac failure to "sudden peripheral obstruction in the circulation and degenerative changes in the cardiac muscle." Later he added another case in which there was neither scarlet fever nor dropsy.[2] Clinically the area of

cardiac dullness was decidedly increased, and at post-mortem, acute nephritis and dilatation of both ventricles of the heart were found. He advised the use of digitalis in the treatment of such cases.

Silberman[3] described five cases in 1881, one terminating in pulmonary edema. Friedlander[4] made similar observations at autopsy. Steffen[5] described another case in which there were dyspnea and cyanosis. In 1889 Hutinel[6] taught that in the absence of cardiac disease, acute dilatation of the heart should be considered diagnostic of acute nephritis. He advised caffein therapy.

During the next twenty years no reference to the subject appeared in the literature, other than passing mention in several textbooks.[7, 8, 9] In 1909 Nobecourt and Voisin[10] described twelve cases of acute nephritis in children. Dilatation of the heart was invariably present. The clinical determination of the size of the heart was made by a percussion method described by Potain. In four of these cases recession of the area of cardiac dullness was found after recovery. These authors also believed with Hutinel that cardiac failure in the absence of a valvular lesion should be considered diagnostic of acute nephritis. Foucault[11] described thirteen similar cases in 1910.

In 1914 Volhard and Fahr[12] wrote a classical description of acute diffuse glomerulonephritis, noting the hypertension, edema, intense dyspnea and orthopnea, over-active heart beat, presystolic gallop, apical systolic murmur, accented apical first sound, diastolic apical thrust, displacement of the apex beat, and widening of the area of cardiac dullness. They stated that the cardiac response appeared greater in cases without edema, and that death could occur solely from pulmonary edema. Only two cases are cited. In 1917 Francke[13] described dilatation of the heart in a series of sixty-nine cases of acute nephritis. Seventy-five per cent of the sixty-seven cases in which x-rays were available showed enlargement of the heart, which he considered to be a combination of hypertrophy and dilatation. Alwens and Moog[14] in 1920 described four cases with serial orthodiagrams showing enlargement of the heart and return to normal on recovery. They thought the enlargement due to acute dilatation and hydropericardium. Assmann[15] questioned this double etiology and both Goodhart and Volhard and Fahr had previously noted the presence of cardiac dilatation without the accumulation of fluid in the tissues and serous cavities.

Finally, Christian and O'Hare[16] in 1925 stated the contrary and entirely erroneous view. Their statement is categorical. "The heart is unchanged by acute nephritis except in a rare case." They further contend that enlargement of the heart or cardiac murmurs or arrythmias in acute nephritis should be regarded as coincident disturbances and that circulatory failure or a good response to cardiac treatment militates against the diagnosis. The weight of evidence is contrary to this opinion.

The physiology of cardiac enlargement in acute nephritis appears to have been best described by Goodhart whose explanation is given above. Volhard and Fahr hold a similar view. Wiggers[17] quotes adequate physiological experiments to confirm these clinical and pathological observations.

The response of the heart to an acute attack of glomerulo-nephritis is made apparent, not only by the circulatory symptoms encountered, but it may also be well visualized by teleroentgenograms. The sooner they are taken after the onset of the attack, the more successful will be the demonstration of acute cardiac dilatation. These facts will be illustrated in ten cases.

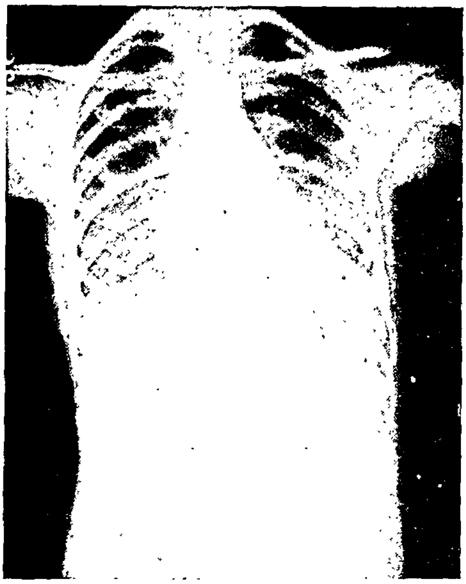

Fig. 1.—Case 1. Two days after onset of symptoms. Dilatation of the heart in all diameters. Congestion of pulmonic fields.

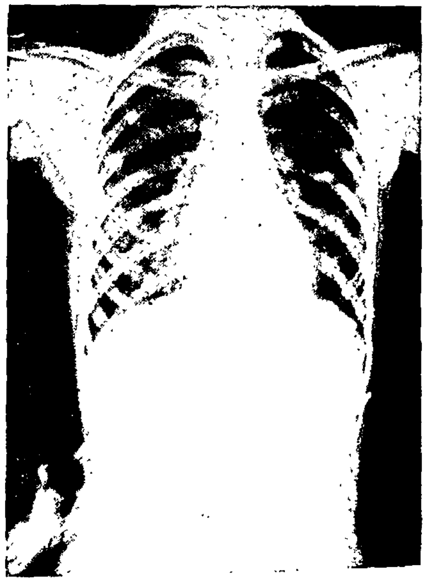

Fig. 2.—Case 1. Twenty-five days after onset of symptoms. Apparently normal in size and contour, but see Fig. 3.

CASE REPORTS

Case 1.—Female, 8 years of age, was admitted to the City Hospital on May 7, 1924. The diagnosis was acute nephritis. Two days before admission she complained of "not feeling well," dyspnea and swelling of the face. The salient points in the physical examination were slight dyspnea, edema of the ankles and face and a loud systolic murmur at the apex of the heart. The blood pressure was 174 mm. systolic and 110 mm. diastolic. The urinary findings were characteristic; albumin, casts, and blood were found. The blood urea nitrogen was 35 mg. per 100 c.c. The child weighed 27 kg. (59.5 lbs.). The phthalein excretion was 40 per cent in the first hour and 30 per cent in the second. She was put to bed without any special medication on a diet consisting of 1500 calories and 25 grams of protein.

At the end of three weeks there was a definite improvement in her clinical condition. The blood urea nitrogen was normal, but the urine still contained blood. The protein in the diet was then increased to 40 grams, and in a few days there was a definite increase in the level of the blood urea nitrogen to 26 mg. per 100 c.c. Again placed on a 25 gram protein diet the nitrogen level in the blood fell to

normal. Later, an increase of the protein to 35 grams produced no increase in the nitrogen level in the blood. She was discharged June 30, apparently normal.

In a few months she was requested to return and was again admitted on September 15. The only positive finding on this date was a trace of albumin in the urine. On a diet containing over 50 grams of protein, no rise in the urea content of the blood occurred.

The first teleroentgenorgram (Fig. 1) was taken two days after the onset of symptoms. It shows the heart dilated in all diameters, more particularly to the right, borders indistinct, and merging into the congested pulmonic fields.

The second teleroentgenogram (Fig. 2) was taken twenty-three days later. At this date all her symptoms had disappeared and the nitrogen content of the blood was normal on a 25 gram protein diet. The blood pressure was normal, and only a slight trace of albumin, but no blood cells were found in the urine. In this teleroentgenogram there is a resumption of the diameters of the child's heart toward normal figures; in fact at this time the heart was regarded as being

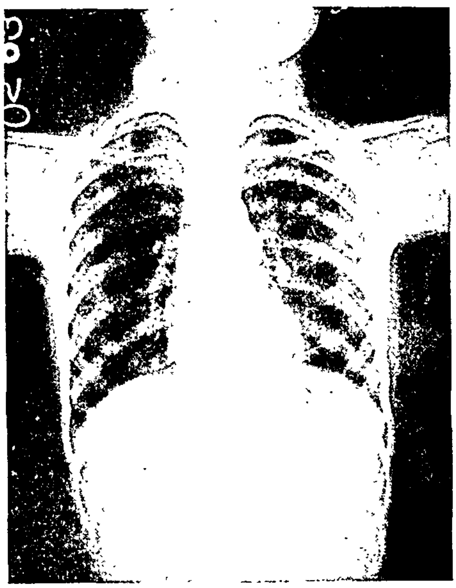

Fig. 3.—Case 1. Three months later. Normal size and contour.

normal in size and contour. The following facts, however, suggested that the pathological process in the kidney was not absolutely healed. When placed on a 40 gram protein diet, the blood pressure and the urea-nitrogen level in the blood were raised, within four days. With a return to the 25 gram protein diet both blood pressure and blood nitrogen returned to normal.

The third teleroentgenogram (Fig. 3) was taken four months after the onset of symptoms. At this date a clinical and metabolic survey of the case suggested complete healing of the renal process. Examination of the plate shows that the diameters of the heart are smaller than on the previous examination, representing the absolute normal size and contour for a child of her age and size. From this we learned that the second teleroentgenogram (Fig. 2) was erroneously interpreted as showing a normal-sized heart. It should be noted that at that time, although the patient's blood pressure at rest was normal, other evidence indicated that the renal process was not healed.

Case 2.—Male, 38 years of age, was admitted to the dermatological service of the City Hospital for an eruption due to pediculosis. He had scarlet fever at the

age of 8 years, at which time he was told he could never be perfectly normal. In 1917 he had influenza with fever and cough. Subsequently he developed a winter cough.

Six weeks after admission a generalized edema developed and he was transferred to the medical service and later to the metabolic service on February 26, 1927. Examination early in February revealed the following facts. He was dyspneic. No murmurs were heard. The blood pressure was 140 mm. systolic and 90 mm. diastolic. Coarse râles were heard over the whole chest posteriorly. On close questioning it was learned that he had noticed some dyspnea on exertion for two and one-half weeks previously. When transferred to the metabolic service he was dyspneic and acutely ill. He weighed 85 kg. (187 lbs.). The urine contained albumin, hyaline, and granular casts and blood. The blood urea nitrogen was 31 mg. per 100 c.c. On the administration of diuretin and a diet containing 25 grams of protein he improved clinically in a short time. He was kept on this diet for about seven weeks, and small doses of digitalis were also given. The blood urea-nitrogen level returned to normal. He lost 20 kg. (44 lbs.). The protein in the diet was increased to 40

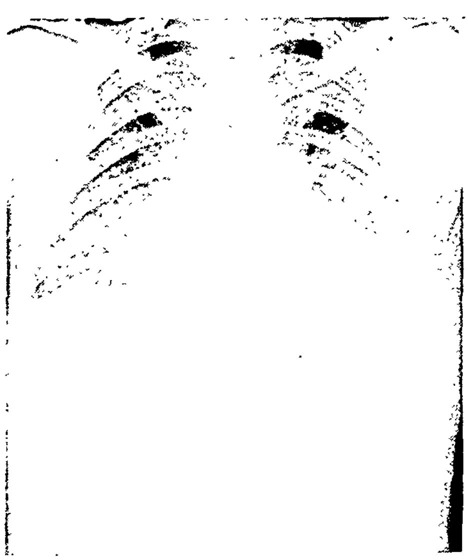

Fig. 4.—Case 2. About three weeks after onset of symptoms. Dilatation of the heart in all diameters. Congestion of pulmonic fields.

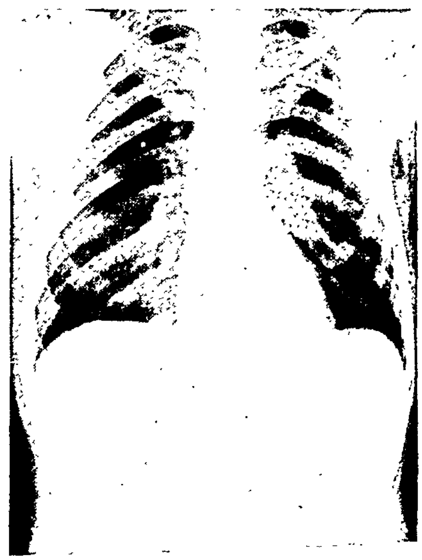

Fig. 5.—Case 2. Three months later. Normal size and contour.

grams and then to 60 grams, both of which were well tolerated. He was discharged May 4, 1927, and took a position as orderly in the hospital.

The first teleroentgenogram (Fig. 4) was taken about three weeks after the appearance of the first symptoms. The heart was dilated enormously in all diameters, with obliteration of the right costophrenic sinus and marked congestion of the lungs. A teleroentgenogram taken three months later shows an unusual transformation (Fig. 5).

Case 3.—Male, 38 years of age, was admitted to Bellevue Hospital on February 22, 1927, for erysipelas of the face and legs. One week later he was discharged as cured. Four days after this he noticed swelling of the legs, ankles and face. He had a slight cough and complained of indigestion. Returning to Bellevue Hospital he was later transferred to the City Hospital and admitted to the metabolic service on April 12.

The heart was apparently normal. The blood pressure was 120 mm. systolic and 80 mm. diastolic. The urine contained albumin and blood. The blood urea nitrogen

was 28 mg. per 100 c.c. He was given a 25 gram protein diet for four weeks. The blood urea nitrogen at the end of this time was 17 mg. per 100 c.c. The diet was increased to 40 grams of protein, then to 60 grams, and finally to 100 grams, which was tolerated very well. He was discharged in good health.

Fig. 6.—Case 3. One month after onset of symptoms. Maximum right horizontal diameter 4.6 cm. Maximum left horizontal diameter 10.3 cm. Pulmonic fields 30 cm.

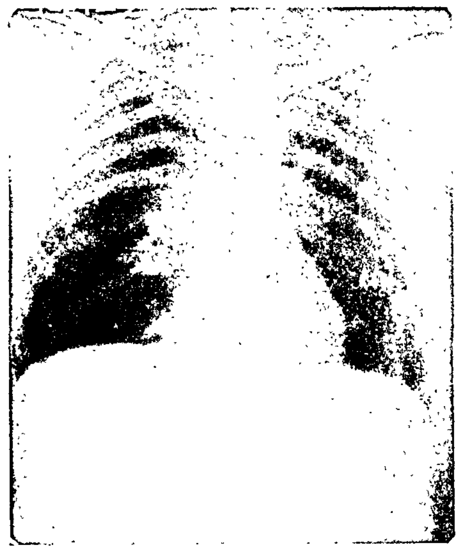

Fig. 7.—Case 3. Thirteen days later. Slight reduction in size of heart. Maximum right horizontal diameter 4 cm. Maximum left horizontal diameter 9.3 cm. Pulmonic fields 30 cm.

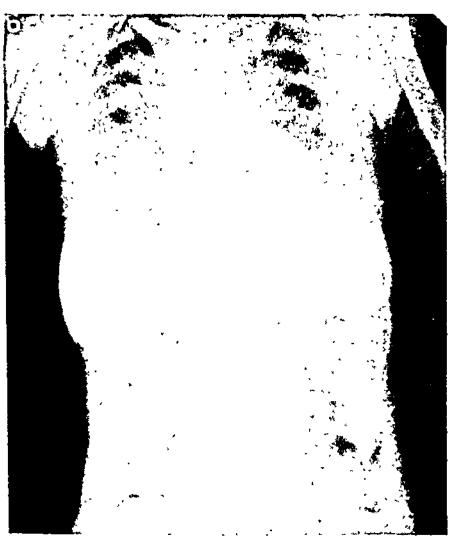

Fig. 8.—Case 4. Six days after onset of symptoms. Dilatation of heart in all diameters. Congestion of pulmonic fields.

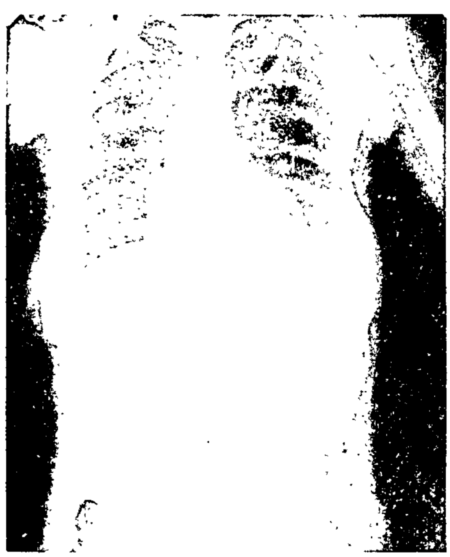

Fig. 9.—Case 4. Fifteen days after onset of symptoms. Slight decrease in size of heart. Borders distinct. Pulmonic fields clear.

The first teleroentgenogram (Fig. 6) was taken one month after the onset of symptoms. Two weeks later when his blood pressure was normal and when there were no red blood cells in the urine and the patient appeared clinically well, the second teleroentgenogram (Fig. 7) was taken. It shows a reduction, though slight, in the size of the heart, from which it must be concluded that even one month

after the onset of symptoms the heart had not returned to its normal size. This indicates that the size of the heart may be an index to the progress of the renal pathology.

CASE 4.—Female, 20 years old, fainted while going to work. She had felt a "shortness of breath" for a few days prior to this. Two days later she was admitted to the hospital. There was a blowing systolic murmur at the apex of the heart. The blood pressure was 190 mm. systolic and 130 mm. diastolic. There were a few crackling râles at the bases of the lungs. The liver was percussed to three fingers below the costal margin and was tender. The extremities were not edematous. Although the urine contained albumin, there were no red blood cells. The blood urea nitrogen was 40 mg. per 100 c.c. She was placed on a 25 gram protein diet. At the end of one week the blood urea nitrogen fell to 24 mg. per 100 c.c. The blood pressure decreased to 150 mm. systolic and 100 mm. diastolic. During the following week she insisted on being discharged.

The first teleroentgenogram (Fig. 8) was taken six days after the appearance of symptoms. It shows the usual cardiac dilatation and pulmonic congestion. The

Fig. 10.—Case 5. Taken in prone position at less than six feet distance from target. Three weeks after onset of symptoms. Bronchopneumonia in right upper lobe. Dilatation of the heart.

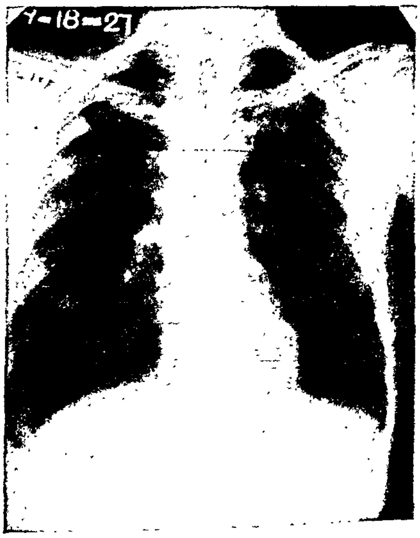

Fig. 11.—Case 5. Usual technic for teleroentgenogram. Six days later. Heart normal in size and contour.

second teleroentgenogram (Fig. 9) was taken nine days after the first. The heart is reduced in size although not normal, and the pulmonic fields are considerably clearer. At this time although the patient was symptom-free, the blood pressure was still elevated. That the renal lesion was not entirely healed is shown by the failure of the cardiac shadow to return to normal dimensions and contour, as well as by the hypertension and disturbance of the nitrogen metabolism.

CASE 5.—Male, 51 years old, was admitted to the medical service on April 10, 1927. He was in good health until about three weeks before admission when he complained of dyspnea. His chief complaints, however, were generalized aches and pains throughout the body. Physical examination showed enlargement of the heart to the left, a loud systolic murmur at the apex of the heart, and blood pressure 140 mm. systolic, 90 mm. diastolic. The liver was enlarged and tender, and the legs slightly edematous. The physical signs in the chest were such as to suggest a diagnosis of confluent bronchopneumonia. The temperature fluctuated between 101° and 103° F. There were albumin, casts and blood in the urine.

Large doses of caffein were administrated for nine days, at which time he was seized with general convulsions. It was questionable whether these were due to the caffein administered or to uremia.

On April 19, 1927, the patient was transferred to the metabolic service. Within a few days, although the dyspnea subsided, the blood urea nitrogen gradually increased to 64 mg. per 100 c.c. He began to show signs of chronic uremia. Treatment was with forced fluids and a negligible nitrogen intake. After several days the blood urea nitrogen decreased and clinical improvement was evident. He received a 25 gram protein diet for about five weeks, the blood urea nitrogen falling to 18 mg. per 100 c.c. The diet was then increased to 60 grams of protein and finally to 80 grams, this amount of nitrogen being fairly well borne.

The first roentgenogram (Fig. 10) was taken about three weeks after the onset of symptoms. Unfortunately it was a chest plate. It shows a suspicious patch of bronchopneumonia in the right upper lobe and a dilated heart.

A teleroentgenogram (Fig. 11) was taken one week later. Although these two roentgenograms are not absolutely comparable, there is little question that the

Fig. 12.—Case 7. Ten days after onset of symptoms. Maximum right horizontal diameter 4.5 cm. Maximum left horizontal diameter 9.9 cm. Pulmonic fields 26.8 cm.

heart was definitely dilated at the time of the first and that in one week it had resumed its normal size and contour. To bring about similar changes in other cases required a much longer period, and it is our impression that in this case the free use of caffein was responsible for the excellent results achieved.

Case 6.—Male, 22 years old, was in a hospital for one month in 1918 because of "grippe." He worked until September, 1926, when he had an attack of pleurisy and pneumonia. Three weeks later his ankles were swollen, and later the edema involved the entire body. He did not have dyspnea. He entered Bellevue Hospital when he discovered blood in his urine. Within six weeks the edema had disappeared but he was anemic. A blood transfusion was followed by a severe reaction.

He was admitted to the metabolic service of City Hospital on March 5, 1927. Examination revealed anemia, slight edema of the extremities, a blood pressure of 150 mm. systolic and 90 mm. diastolic. The urine contained blood. The urea nitrogen of the blood was 31 mg. per 100 c.c. He was put to bed, given the usual medication and a 25 gram protein diet, the latter being continued for several

weeks until the blood urea nitrogen was normal. The diet was increased to 40 grams of protein, but every attempt to further increase the protein content of the diet met with an increase of blood urea nitrogen to above normal figures. He felt much better but there was little improvement in the anemia.

The first teleroentgenogram was taken about six months after the appearance of the initial symptoms. Two months later very little change in size and contour was found. This suggests that during the period from the onset of symptoms until his admission to the metabolic service he had completely recovered from the acute circulatory decompensation, although he was suffering with the outstanding symptoms of chronic glomerulonephritis.

Case 7.—Male, 24 years old, was admitted to the nose and throat service of the City Hospital for recurrent epistaxis which had persisted intermittently for ten days. On close questioning he admitted that during this period he was dyspneic and had slight edema of the extremities. His face was pallid. A systolic murmur was heard at the apex of the heart. Both pulmonary bases were

Fig. 13.—Case 7. Three weeks later. Maximum right horizontal diameter 4 cm. Maximum left horizontal diameter 8.4 cm. Pulmonic fields 27.9 cm.

filled with numerous râles, and the breath sounds throughout the lungs were sibilant. The liver could be percussed to three fingers below the costal margin but was not tender. The fundus was normal. The urine contained granular and hyaline casts and blood. The blood urea nitrogen was 88 mg. per 100 c.c. The blood count revealed an anemia and leucocytosis, viz., hemoglobin 45 per cent, R.B.C. 3,250,000, W.B.C. 13,800. The blood pressure was 150 mm. systolic and 80 mm. diastolic. He was transferred to the metabolic service on May 5, 1927, given the usual medication and a 25 gram protein diet for about four weeks. The blood urea nitrogen diminished to within normal limits, and the diet was accordingly increased to 60 grams of protein and finally to 80 grams with no retention of nitrogen in the blood.

The first teleroentgenogram (Fig. 12) was taken ten days after the onset of symptoms. It shows the usual dilated heart. One taken almost three weeks later demonstrated that the heart had returned to its normal size and contour (Fig. 13). The patient at this date had not entirely recovered. The urea-nitrogen level in the blood was slightly elevated on a 25 gram protein diet, although the urine was normal.

CASE 8.—Male, 49 years old, was admitted to the medical service because of dyspnea and orthopnea. He was in great distress. The diagnosis was general arteriosclerosis and cardiac decompensation. An outstanding feature of the case was the enlargement and tenderness of the liver. The urine contained albumin, a few granular casts and many pus cells. Two days after admission the blood urea nitrogen was 12 mg. per 100 c.c. Nine days later it was 23 mg. per 100 c.c. He died within one month with all the symptoms of circulatory decompensation.

Post-mortem Examination: The heart weighed 670 grams and showed evidence of chronic myocarditis. The left ventricle was thickened, the right ventricle and auricle were enormously dilated. The coronary arteries and heart valves were normal. The kidneys each weighed 300 grams. The line of demarcation between cortex and medulla was absent. Histological examination of the kidney revealed arteriosclerosis and acute diffuse glomerulonephritis.

The teleroentgenogram (Fig. 14) shows a heart dilated enormously in all diameters, particularly to the right. The interesting feature of this case is the presence of acute glomerulonephritis without definite evidence in the urine or blood.

Fig. 14.—Case 8. Dilatation of the heart in all diameters.

The acute dilatation of the heart, particularly to the right, and the large and tender liver, without any endocardial, pericardial or coronary cause, should have led one to suspect that the basis of this acute dilatation was acute nephritis.

CASE 9.—Male, 39 years old, was admitted to the medical service about two weeks after the onset of symptoms. He complained of pain in the legs and abdomen and of shortness of breath for ten days. Then he noticed edema of the extremities. Physical examination revealed general anasarca, a systolic murmur at the apex of the heart and absence of breath sounds at the bases of the lungs. The blood pressure was 270 mm. systolic and 120 mm. diastolic. Scattered throughout both retinas were numerous hemorrhages and a few white exudative areas. The margins of the optic discs were fairly sharp. The blood urea nitrogen was 40 mg. per 100 c.c. The urine contained blood. Under the usual medical and dietetic régime he improved greatly. The blood pressure dropped to 128 mm. systolic, the body weight decreased 15 kg. (33 lbs.), and the urine was free of blood.

The first teleroentgenogram was taken two weeks after the onset of symptoms. The second taken two weeks later shows a slight but appreciable change.

CASE 10.—Female, 19 years old, came to my office June 16, 1924, complaining of puffiness of the legs and face which was noticed the previous day. She had had an aching precordial pain for two days, although there was neither dyspnea nor palpitation. Two weeks previously she had an attack of follicular tonsillitis and developed a cough but gradually improved. The heart was slightly overactive but otherwise negative. The blood pressure was 115 mm. systolic, 80 mm. diastolic. The liver was palpable three fingers below the costal margin and distinctly tender. The lungs were not congested. The fundus was normal. The urine showed a trace of albumin, granular and hyaline casts and several red and white blood cells to each microscopic field. The blood urea nitrogen was elevated; 52 mg. per

Fig. 15.—Case 10. Two days after onset of symptoms. Maximum right horizontal diameter 4.3 cm. Maximum left horizontal diameter 6.7 cm. Pulmonic fields 24.5 cm.

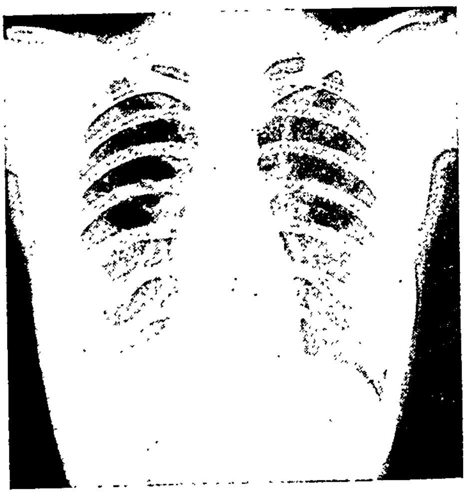

Fig. 16.—Case 10. Twenty-six days after onset of symptoms. Maximum right horizontal diameter 3.3 cm. Maximum left horizontal diameter 5.5 cm. Pulmonic fields 24.5 cm.

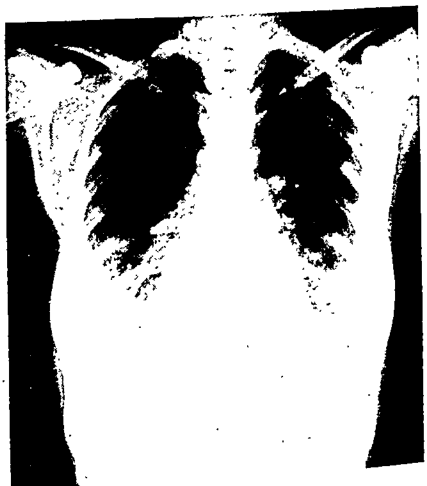

Fig. 17.—Case 10. Almost three years later. Maximum right horizontal diameter 4.6 cm. Maximum left horizontal diameter 6 cm. Pulmonic fields 25 cm.

100 c.c. Although the patient felt no discomfort, she appeared dyspneic. She was sent home and put to bed for three weeks on the usual medication and dietetic treatment, she improved greatly. On July 10 the urine was normal. The blood urea nitrogen was 19 mg. per 100 c.c. The blood pressure was 100 mm. systolic and 60 mm. diastolic.

After an interval of almost three years she again presented herself for examination, stating that she had slight pain over her heart when tired. No abnormalities were found on physical examination.

A teleroentgenogram (Fig. 15) taken two days after the onset of the circulatory symptoms demonstrated the dilatation of the heart in all diameters, particularly to the right. It should be noted that at this date her blood pressure was normal. A teleroentgenogram (Fig. 16) taken after all symptoms had subsided showed the heart practically normal in size and contour for a girl of her physique. The third teleroentgenogram (Fig. 17) taken almost three years later showed the heart to be definitely larger than in 1924.

There are several interesting features in this case. Although the patient was undoubtedly suffering with acute glomerulonephritis and showed a dilated heart in the teleroentgenogram, her blood pressure was not elevated. The interpretation of the cardiac enlargement three years later is not a simple matter. It may have been due to the normal growth of the heart in a girl who had advanced three years in age and over twenty pounds in weight, or it may have been the result of a latent chronic glomerulonephritis which presented no other symptomatology.

I am unable to present any conclusive data as to the electrocardiographic abnormalities in acute nephritis.*

SUMMARY

The recognition of the presence of acute circulatory decompensation is extremely important in the diagnosis and treatment of acute diffuse glomerulonephritis. The cardinal symptoms, namely, hypertension, edema, hematuria and renal insufficiency as shown by nitrogen retention in the blood, may be absent. The pathology in the kidney consequently may not be detected. Cases of this description are reported in this series. The only clue to the diagnosis is obtained by a proper interpretation of the circulatory symptoms. The sudden advent of circulatory decompensation as evidenced by dilatation of the right side of the heart, pulmonary congestion, and an enlarged and tender liver should lead one to suspect the presence of acute nephritis. This applies particularly in cases in which valvular or coronary artery lesions are absent and no other cause for decompensation can be found. Although it is generally believed that the edema in acute diffuse glomerulonephritis is a "tissue disturbance," caused by some derangement of general metabolism, the fact must not be overlooked that water retention may also be due to the circulatory disturbance. The determination of this point is of extreme importance in deciding upon the form of therapy to be pursued. Pulmonary edema may be the cause of death in acute nephritis. It may occur even though the structural changes in the kidney are not sufficient to produce complete renal insufficiency. The early recognition of the etiology of the circulatory symptoms may be the means of saving life. In addition to dietetic measures, proper cardiac supportive treatment should be undertaken. Often, rest in bed will suffice. The liberal use of caffein products such as diuretin, theocalcin and caffein sodium benzoate, and digitalis are indicated.

*Electrocardiograms were taken in seven of these ten cases. In three (Cases 2, 5 and 6) there are no significant abnormalities. In one case (Case 10) the T-wave is unusually high and pointed in Leads I and II. In the remaining three cases (Cases 4, 8 and 9) inversion, diphasic character or flattening of the T-waves in Leads I and II are present, but all had received some digitalis. Other cases seem to indicate the presence of abnormalities of the T-wave in some stage of the disease.

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CHARACTERISTIC ELECTROCARDIOGRAMS AND ROENTGENOGRAMS IN ARTERIAL HYPERTENSION

Their Prognostic Significance*

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THE electrocardiographic and roentgenographic changes in patients with arterial hypertension have been found to be so characteristic and their relations to the clinical findings of such prognostic value that it has been deemed advisable to report them. When one considers that an individual may have marked hypertension for from twelve to fifteen years before developing definite symptoms of myocardial failure, any aid to prognosis, such as the electrocardiogram and the roentgenogram, is of value. Fahr[1] and others have recently emphasized the prevalence and chronicity of hypertension.

The 152 patients studied† were those with blood pressures habitually above 160 mm. systolic, and 90 mm. diastolic. By far the greater number had essential hypertension, only 10 per cent were associated with nephritis. The data cover a period of at least three years and a follow-up system has kept the records up to date. One or more electrocardiograms were taken in every case and in 106 patients, one or more teleroentgenograms.

Ninety-two of the patients were females and 60 were males. The ages ranged from eleven to eighty years; 18 patients were under forty, 29 patients were between forty and fifty, 50 patients were between fifty and sixty, 28 patients were between sixty and seventy years of age.

The literature on the electrocardiographic changes in hypertension is very meager. Einthoven[2] noted an inversion of the main deflection of the QRS group in the third lead in patients with hypertrophy of the left ventricle. Linetzky[3] was the first to study the effect of high blood pressure on the electrocardiogram. He discovered that with an augmentation in blood pressure the R-wave increased in amplitude while the T-wave diminished. He stated that the T-wave was usually negative in patients with a systolic blood pressure over 230 mm. His belief was that hypertension caused an enlarged heart and that the latter produced these electrocardiographic changes. Lewis,[4] in 1913, concluded that "high blood pressure appears to be especially potent in creating a preponderance of the left ventricle." Munk[5] mentioned tall R-waves, negative T-waves in Lead I, premature beats and auricu-

*Read before the Section on Internal Medicine, New York Academy of Medicine, March 19, 1929.

†Through the courtesy of Dr. B. S. Oppenheimer of New York, the data here presented were taken for the most part from his private records. In about ten cases the records of Mount Sinai Hospital, New York, were also utilized.

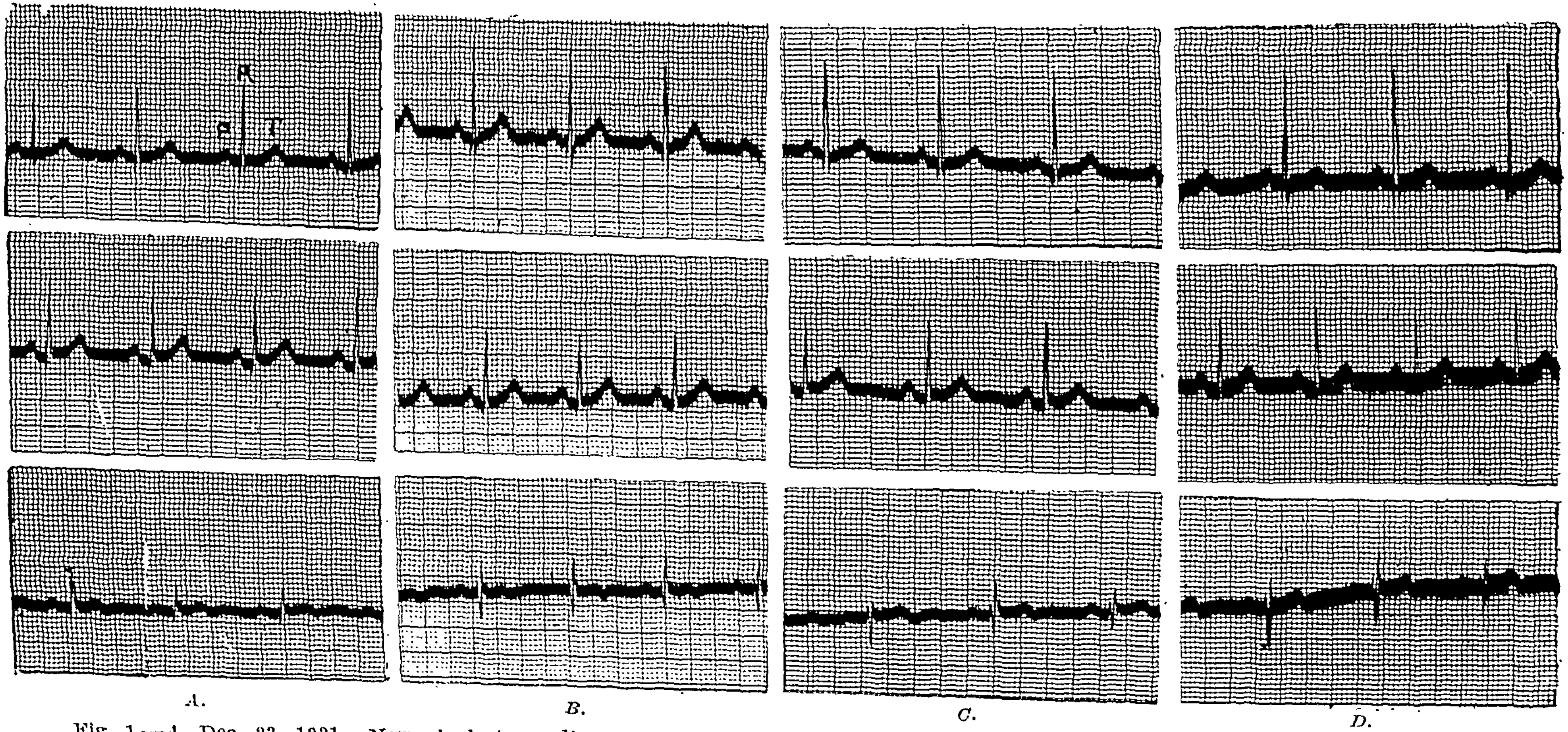
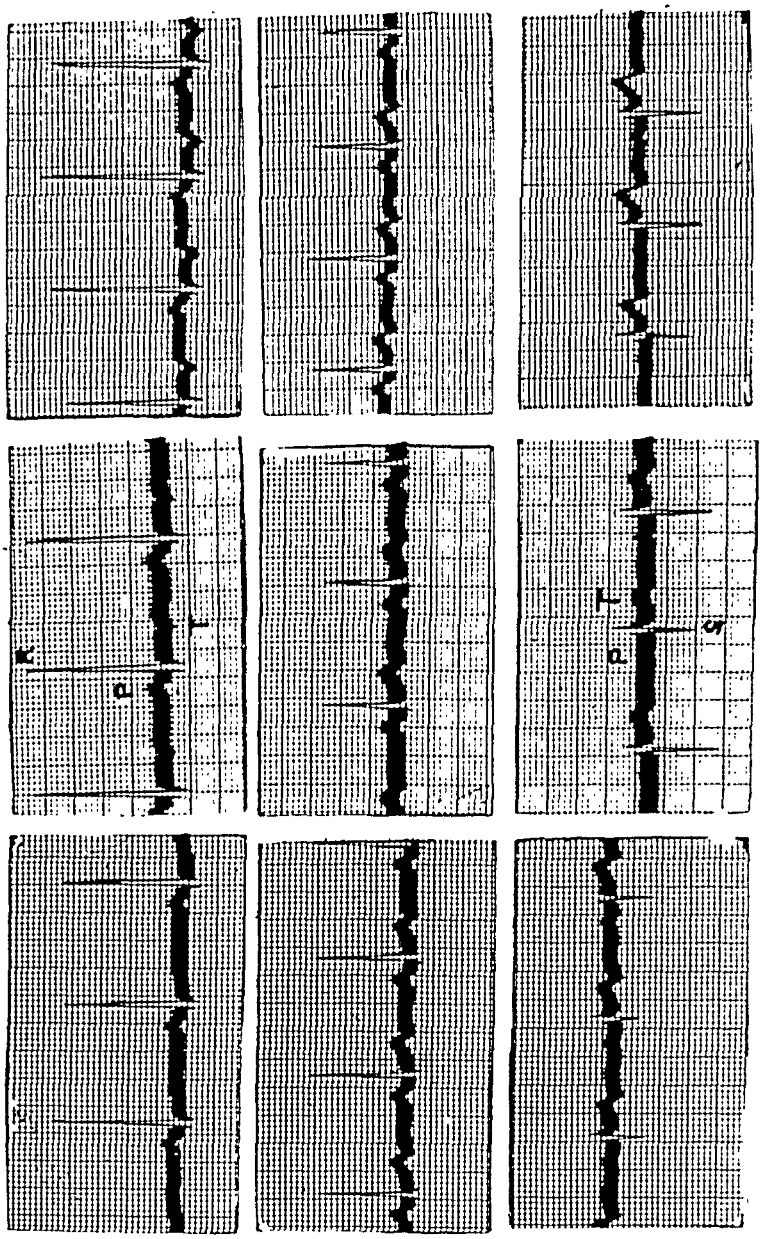


Fig. 1.—A, Dec. 23, 1921. Normal electrocardiogram. Age of patient fifty-nine years; B, Mar. 8, 1923. Blood pressure 150/90. Development of a moderate left axis deviation. Increase in amplitude of R- and S-waves; C, Dec. 29, 1923. Blood pressure 152/90. More definite left axis deviation; D, Oct. 26, 1925. Blood pressure 200/90. Further increase in voltage of QRS group; E, Nov. 10, 1927. Blood pressure 170/100. T-wave in Lead I flat (isoelectric); F, Mar. 25, 1928. Blood pressure 178/100. Further increase in voltage of QRS group. T-wave in Lead I slightly inverted; G, Nov. 1, 1928. Blood pressure 174/104. T-wave in Lead I definitely inverted.

lar fibrillation as occurring in hypertension. White and Burwell[6] studied unselected cases of hypertension and found from 44 to 47 per cent of the patients to have left axis deviation of the QRS group, i.e., a left ventricular preponderance. Their percentages were smaller than my own.



E. F. G.

Fig. 1.—Cont'd

ELECTROCARDIOGRAPHIC STUDIES

The most common change found was that of the left axis deviation. This was present in 112 persons out of a total of 152, i.e., 74 per cent (Fig. 1, *C, D, E, F, G*). This is a decided increase over normal figures in the same age groups, and constitutes, therefore, a definite electrocardiographic finding in hypertension cases. Twenty-three of these

patients died, a percentage of 21, whereas the general mortality rate of all the patients for three years was 18 per cent.

The second most common finding was a combination of left axis deviation with inversion of the T-wave in Lead I (Fig. 1, *G*). This occurred in 36 per cent of the cases. The serious import of the inverted T-wave is readily appreciated when its frequent association with coronary artery disease and myocardial involvement is recalled. The mortality rate in this group was 27 per cent. Every case of T-wave inversion in the first lead was associated with a left axis deviation of the QRS group.

The third most common change seen in the electrocardiograms of hypertension patients was a combination of high voltage of the QRS group, a left axis deviation, *inversion of the T-wave in the first lead,* and shortening or disappearance of the R-T or S-T intervals (Fig. 1, *G*). The amplitude of the waves of the QRS group is usually 18 millimeters or more in at least one lead. The duration of the QRS waves is usually within the normal limits, i.e., 0.10 second, but 0.12 second in a case with high voltage must be considered normal. In general the T-waves are directed oppositely to the main deflection. For descriptive purposes this type of record has been called the high-voltage electrocardiogram in hypertension.

The development of the high-voltage electrocardiogram is gradual, and is related rather to the duration of the hypertension than to the height of the blood pressure. Fig. 1 illustrates the case of a woman now sixty-seven years of age who has had hypertension for at least eight years. The normal record gradually changes to a left axis deviation, then there occurs an increase in voltage of the QRS group with development of inversion of the T-waves in the first and second leads. The R or S-T interval shortens or disappears entirely.

All patients in the "high voltage" group who have had numerous electrocardiographic tracings showed changes over a period of years. Fourteen patients were followed from two to nine years. When the investigation was conducted over a sufficient period of time and if records were taken frequently enough, every one of these changes was usually noted; at other times there occurred a change from a normal tracing to one with a left axis deviation, a change from a normal voltage of the R- and S-waves to one of high voltage, or from an upright T to an inverted, or a combination of all of these.

The high-voltage electrocardiogram in hypertension occurred in 33 patients. The mortality among these was very high—40 per cent for three years.

Twenty-six of these patients were roentgenographed. Sixteen of these showed a dilated ascending aorta and 24 showed evidences of a definite concentric hypertrophy of the left ventricle. In other words

the high-voltage electrocardiogram in hypertension is associated with the x-ray changes usually seen in hypertension.

ROENTGENOGRAPHIC STUDIES

Coincidentally with the electrocardiograms, teleroentgenograms were taken on 106 patients.

Munk[5] and Vaquez and Bordet[7] have described the heart in hypertension. They speak of an elongated, tortuous aorta, of a left ventricle that is hypertrophied, and of a heart in which the longitudinal

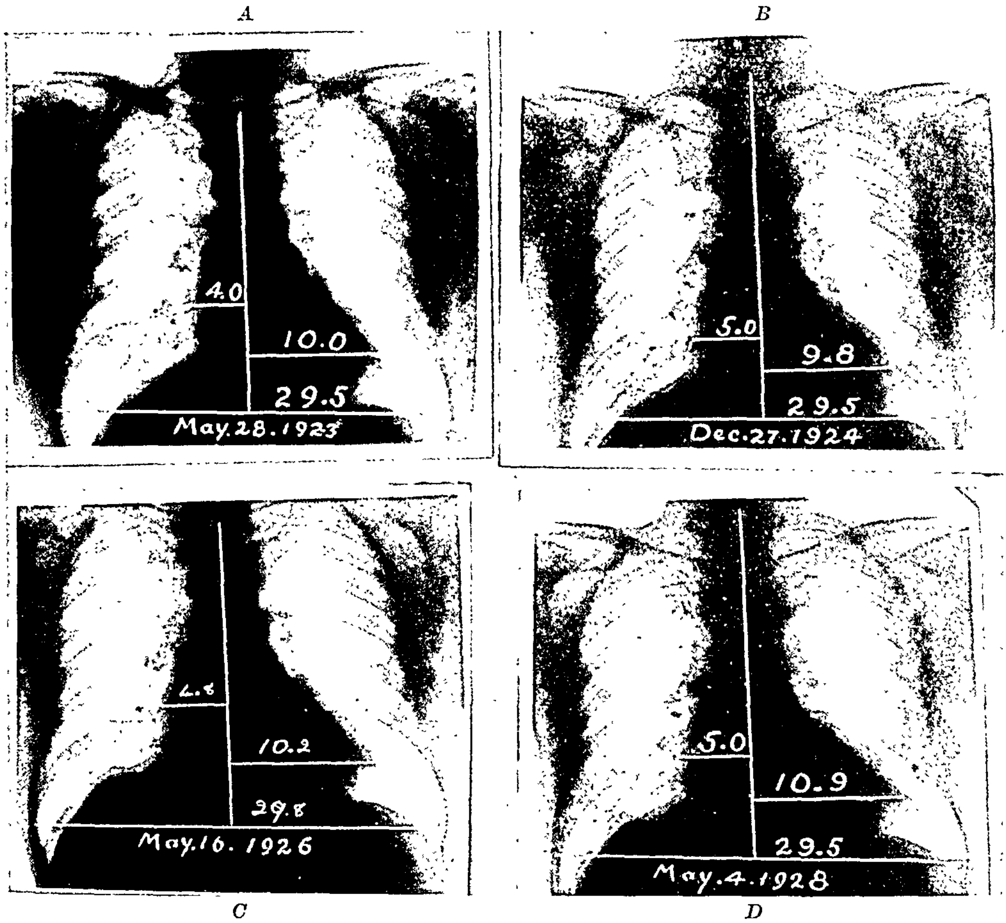


Fig. 2.—*A*, Blood pressure 158/100. A practically normal heart. (Slight hypertrophy of left ventricle); *B*, Blood pressure 166/100. Heart enlarged. Left ventricular hypertrophy. Tortuous aorta, prominent aortic knob. *C*, Blood pressure 160/100. A further left ventricular hypertrophy. *D*, Blood pressure 170/110. A marked left ventricular hypertrophy with rounded apex.

and transverse diameters may become considerably increased. Munk gives diagrammatic illustrations of changes in the aorta and left ventricle.

The habitus of this group was also studied. The criteria here used are those proposed by Groedel,[8] and Hirsch and Shapiro.[9] Six patients belonged to the hypersthenic, 77 to the sthenic, and 23 to the hyposthenic type. It is usually the sthenic or hypersthenic type of individual that develops hypertension.

The left ventricle was hypertrophied and more or less sharply outlined in at least 48 per cent of the cases. This fact added no prognostic significance to the clinical history. A left ventricle hypertrophy by x-ray film was usually associated with a left axis deviation by the electrocardiogram, but a left axis deviation did not necessarily indicate a hypertrophy of the muscle chamber, as seen in the x-ray picture.

The shadow of the ascending aorta was definitely widened (Figs. 2 and 3) in 23 patients, and slightly widened in 11 more. The mortality among these patients was slightly higher than the average—22 per cent for the three years. This dilatation of the aorta is more apparent than real in that the vessel which appears somewhat to the right can be shown by fluoroscopy or by sagittal-view roentgenogram to be tortuous rather than dilated. Munk[5] and Vaquez and Bordet[7] have called attention to this point.

The hypertension roentgenogram is characterized by the sthenic or hypersthenic type of chest, the hypertrophied left ventricle, the

Fig. 3.—Tortuous aorta. Aortic knob prominent. Left ventricular hypertrophy.

enlarged heart, the dilated or tortuous aorta, and the prominent aortic knob (Figs. 2, *C*, *D*, and 3). These late changes in the heart and aorta are indicative of a previous long-standing hypertension. Fig. 2 shows the progressive changes in the size, shape, and position of the heart and aorta in a case of chronic hypertension, beginning with a practically normal heart.

DISCUSSION

The explanation of the three common electrocardiographic findings in hypertension, namely, (1) left axis deviation, (2) left axis deviation with the T-wave inversion in the first lead, and (3) the high-voltage electrocardiogram in hypertension, probably lies in the size, shape, and position of the left ventricle, or, more accurately, in the length and direction of the specific conduction pathways. Cohn[10] in experiments on human beings, and Meek and Wilson[11] in experiments on dogs, have shown that change in position and rotation of the heart may alter the axis deviation and transform a positive T-wave into a negative one. The time relations, i.e., the onset of excitation of the

bundle branches; the length and direction of this excitation in each bundle branch, and the change, if any, in the time of retreat of the conduction wave or in its direction, are all important factors with respect to the fixed leads.

When one considers specifically the inversion of the T-wave, the same explanation is at hand, but the possibility of coronary artery disease must be considered. Patients with hypertension often have coronary artery involvement. At post-mortem examination these vessels may be found to be markedly diseased. However, the previous explanations may nevertheless hold true, for a coronary artery occlusion with its resultant thrombosis probably throws out of balance the electrical pathways of the right and left ventricles. Moreover, it has been suggested that following a closure, a change in size, shape, and rotation of the left ventricle may account for the inverted T-wave.[12] Luten and Grove[13] believe that records with a left axis deviation, inversion of the T-wave in Lead I and normal QRS groups are caused by defective conduction in the right limb of the A-V bundle and that this defective conduction is due to disease of the left coronary artery. The evidence at hand, however, tends to show that if hypertension in a patient with the high-voltage electrocardiogram persists long enough, the T-wave will eventually become inverted and remain so, whether or not coronary artery disease be present. Again, this typical electrocardiogram, with the marked left axis deviation and inversion of the T-wave in Lead I, is very occasionally seen in young children with a pure aortic insufficiency of rheumatic origin where there is no question of coronary artery disease. Moreover, the T-wave of the high-voltage record is deeper and narrower than that of the inverted T of the ordinary coronary artery closure case. Finally, it seems that once this T-wave becomes inverted it remains so, whereas in recovery from a closure of the coronary artery the patient is apt to lost the negativity of his T-wave.

The high-voltage electrocardiogram in hypertension, as described in this paper, was first called the "hypertension electrocardiogram"[14] but the use of this term is open to criticism since these electrocardiographic changes have occasionally been seen in uncomplicated cases of aortic insufficiency.

It must be emphasized that not every patient with hypertension will show either this high-voltage electrocardiogram or the hypertension x-ray picture. The converse is true nevertheless, that these graphic changes, if present in a patient who has no aortic insufficiency, indicate that the patient must have had arterial hypertension for many years.

High voltage of the QRS group alone, i.e., with no T-wave inversion, was not included among the significant changes, although it is believed

that the positive T-wave ultimately becomes inverted. It is probably an early stage of the high-voltage electrocardiogram in hypertension.

A word must be said of the possible clinical significance of the high-voltage record as well as the hypertension roentgenogram. I believe that they indicate a long-standing hypertension even when there is no history or current clinical evidence of it. Such an electrocardiogram has been seen in patients with coronary artery disease who have lost their hypertension. A clinical study is at present being made of patients who yield these high-voltage electrocardiograms, and it seems probable that these records may give as much evidence to the clinician of a previous long-standing hypertension as does the hypertrophied left ventricle at the autopsy table to the pathologist.

SUMMARY

The electrocardiographic and teleroentgenographic records of 152 patients with hypertension have been studied. The general mortality among these patients, covering a follow-up of three years, was 18 per cent.

Seventy-four per cent of the patients showed left axis deviation in the electrocardiogram. This is therefore a common change in hypertension cases. However, it does not necessarily indicate a left ventricular hypertrophy by x-ray picture.

The next most common finding was a combination of left axis deviation with T-wave inversion in the first lead. This occurred in 36 per cent of the cases. The mortality rate in this group was 27 per cent.

Every case of T-wave inversion in the first lead was associated with left axis deviation.

The high-voltage electrocardiogram in hypertension was present in 22 per cent of all the cases. Among these patients the mortality was high—40 per cent. This electrocardiogram, when pure aortic insufficiency is not present, appears to be characteristic of long-standing hypertension. A gradual change in the size, shape, and position of the left ventricle probably accounts for the electrocardiographic findings.

Of 106 patients in whom teleroentgenograms were taken, 78 per cent belonged to the so-called sthenic or hypersthenic types of habitus.

The hypertension roentgenogram, characteristic of long-standing hypertension, shows an enlarged heart, an hypertrophied left ventricle, and an apparently dilated but actually tortuous aorta, with a prominent aortic knob.

The left ventricle appeared hypertrophied on the roentgenogram in 48 per cent of the patients. In each case a left axis deviation was present in the electrocardiogram.

The ascending aorta was apparently widened in 32 per cent of the cases. Accurately speaking the aorta is not widened but is tortuous.

The "high-voltage electrocardiogram" or the "hypertension roentgenogram" may be the only existing evidence of a previously long-standing hypertension.

I wish to express my sincere thanks to Dr. B. S. Oppenheimer, Dr. H. Wessler and to Dr. L. A. Conner for their helpful suggestions. I am indebted to Miss Lydia Bucchi for her kind assistance.

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STUDIES ON THE EFFECT OF NITROGLYCERIN, AMYL NITRITE AND ACETYLCHOLINE ON HYPERTENSION*

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THE medicinal treatment of hypertension is frequently unsatisfactory and the results, when obtained, are often only temporary. The resulting disappointment is due in great part to adherence to the widespread and traditional belief that nitrites and other substances reduce blood pressure regardless of the cause. Much of the clinical evidence upon which this belief is maintained is based on observations not properly controlled, and reduction in blood pressure is frequently due in great part to such factors as rest in bed, diet, and limitation of fluid intake rather than to the effect of the drugs used.

In view of the contradictory reports in the literature on this subject it was decided to study the effect of nitroglycerin, amyl nitrite, and acetylcholine (acecoline) in a selected and controlled group of cases. The acetylcholine was obtained directly from the Anglo-French Drug Company, the nitroglycerin and amyl nitrite were taken from the hospital supply.

METHOD OF STUDY

Ten patients with hypertension and renal involvement were selected for this experiment and 10 additional normal persons were used as controls. The hypertension patients were first examined physically for clinical evidences of renal disease. The average concentration of urea in the blood was 30 mg. per 100 c.c. and the average creatinine was 2.5 mg. The urine was of low specific gravity with little variation during the day or night. The night urine averaged about 900 c.c. The power of concentration, dilution, and excretion of water was impaired in all patients. The blood pressure averaged 195 mm. of mercury.

All patients were kept in bed on a low protein and salt poor diet and the total fluid intake was limited to 1500 c.c. in twenty-four hours. The blood pressure was taken twice a day by the auscultatory method, using a mercury manometer. The drugs were not given until the blood pressure was reduced to a fixed level by this management, in order to exclude the factors of rest, diet, and limitation of fluid intake. All three drugs were used on each of the patients and on the controls at suitable intervals in order to compare their effects on the same

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individual. After administration of the drugs, blood pressure readings were made every two minutes for an hour and then at frequent intervals for the next twenty-four hours.

RESULTS

Nitroglycerin, gr. $\frac{1}{50}$, was given under the tongue to 10 normal persons after the blood pressure level was previously established. The maximum effect occurred in two minutes, the average maximum drop of the systolic pressure was 18 mm., and the average reduction in the diastolic pressure was 6 mm. The systolic pressure remained low for fifteen minutes and was not followed by a rise above the former level, while the diastolic pressure remained below the original pressure for

TABLE I

NORMAL CONTROLS

EFFECT OF NITROGLYCERIN (GR. $\frac{1}{50}$)

TIME ELAPSING BEFORE MAXIMUM EFFECT	MAXIMUM EFFECT	DURATION	REACTION	
			INTENSITY	DURATION
		SYSTOLIC		
2 min.	18 mm.	15 min.	None	None
		DIASTOLIC		
2 min.	6 mm.	9 min.	6 mm.	18 min.

TABLE II

NORMAL CONTROLS

EFFECT OF AMYL NITRITE (2 AMPULES)

TIME ELAPSING BEFORE MAXIMUM EFFECT	MAXIMUM EFFECT	DURATION	REACTION	
			INTENSITY	DURATION
		SYSTOLIC		
4 min.	46 mm.	21 min.	None	None
		DIASTOLIC		
2 min.	38 mm.	20 min.	None	None

six minutes and was often then followed by a rise of from 5 to 8 mm. above the previous normal level. This reaction lasted an average of fifteen minutes. All normal persons showed a fall and subsequent rise very similar to the manner described.

Nitroglycerin, gr. $\frac{1}{50}$, under the tongue was given to 10 patients with hypertension and renal disease after the precautions before mentioned were taken. No effect was observed on the systolic pressure in 3 cases and no drop of the diastolic pressure occurred in 6 instances. The maximum effect on the systolic pressure in the remainder occurred in from two to seven minutes, the maximum fall varied from 4 to 40 mm., and the original pressure returned in from two to eighteen minutes. In 6 cases the pressure rose above the original level, the rise amounting to from 4 to 20 mm. and lasting from two to thirty minutes. The

diastolic pressure dropped in only 4 of the 10 cases. The drop varied from 6 to 14 mm. and lasted from three to twenty minutes. A subsequent rise above the previous level occurred in 6 patients, varying from 8 to 24 mm. and lasting from three to thirty minutes. No subsequent changes were observed during the following twenty-four hours, either in the systolic or diastolic pressures.

Amyl nitrite was administered by inhalation of two ampules held to the nose under a handkerchief. The normal cases showed a maximum drop of the systolic pressure in three minutes amounting to 45 mm. and returning to normal in twenty minutes. The maximum drop in diastolic pressure occurred in two minutes, amounted to 35 mm. and the pressure returned to normal in twenty minutes. No subsequent elevation of either the systolic or diastolic pressures to a level above the previous normal occurred in the control cases in contrast to those seen after nitroglycerin.

TABLE III

HYPERTENSION

EFFECT OF AMYLNITRITE (2 AMPULES) ON SYSTOLIC PRESSURE

CASE NO.	TIME ELAPSING BEFORE MAXIMUM EFFECT	MAXIMUM EFFECT	DURATION	REACTION	
				INTENSITY	DURATION
I	2 min.	56 mm.	8 min.	24 mm.	7 min.
III	3 min.	40 mm.	3 min.	6 mm.	6 min.
IV	2 min.	64 mm.	5 min.	4 mm.	3 min.
V	3 min.	88 mm.	4 min.	10 mm.	8 min.
VI	4 min.	70 mm.	6 min.	None	None
VII	1 min.	108 mm.	5 min.	10 mm.	4 min.
VIII	2 min.	70 mm.	7 min.	None	None
IX	2 min.	42 mm.	5 min.	14 mm.	12 min.
X	3 min.	66 mm.	7 min.	8 mm.	3 min.

TABLE IV

HYPERTENSION

EFFECT OF AMYLNITRITE ON DIASTOLIC PRESSURE

CASE NO.	TIME INTERVAL ELAPSING BEFORE MAXIMUM EFFECT	MAXIMUM EFFECT	DURATION	REACTION	
				INTENSITY	DURATION
I	2 min.	68 mm.	5 min.	8 mm.	5 min.
III	3 min.	12 mm.	3 min.	None	None
IV	2 min.	56 min.	10 min.	14 mm.	10 min.
V	3 min.	86 mm.	5 min.	16 mm.	6 min.
VI	3 min.	46 mm.	7 min.	6 mm.	8 min.
VII	1 min.	62 mm.	10 min.	None	None
VIII	2 min.	30 mm.	6 min.	None	None
IX	2 min.	28 mm.	6 min.	12 mm.	15 min.
X	3 min.	38 mm.	7 min.	None	None

The effect of amyl nitrite on the patients with hypertension was quite marked. The maximum drop in systolic pressure occurred in from one to three minutes, amounted to from 40 to 108 mm., and returned to the previous level in from three to eight minutes. All but

2 of these patients showed a reaction rise above the previous level amounting to from 4 to 24 mm. and lasting from three to twelve minutes. The diastolic pressure fell in from one to three minutes to from 12 to 86 mm. and remained below the original diastolic pressure from three to ten minutes. A reaction rise above the previous level of the diastolic pressure occurred in all but 4 instances amounting to from 6 to 14 mm. and lasting from five to fifteen minutes. Observations during the next twenty-four hours failed to show any appreciable variation in either the systolic or diastolic pressures.

TABLE V

HYPERTENSION

EFFECT OF NITROGLYCERIN (GR. 1/50) ON SYSTOLIC PRESSURE

CASE NO.	TIME INTERVAL ELAPSING BEFORE MAXIMUM EFFECT	MAXIMUM EFFECT	DURATION OF EFFECT	REACTION	
				DURATION	INTENSITY
I	3 min.	12 mm.	4 min.	30 min.	20 mm.
III	7 min.	32 mm.	18 min.	None	None
IV	No effect	No effect	No effect	15 min.	10 mm.
V	5 min.	5 mm.	4 min.	2 min.	5 mm.
VI	No effect	No effect	No effect	None	None
VII	2 min.	4 mm.	2 min.	9 min.	12 mm.
VIII	3 min.	4 mm.	3 min.	12 min.	5 mm.
IX	3 min.	40 mm.	18 min.	None	None
X	No effect	No effect	No effect	10 min.	4 mm.

TABLE VI

HYPERTENSION

EFFECT OF NITROGLYCERIN (GR. 1/50) ON DIASTOLIC PRESSURE

CASE NO.	TIME ELAPSING BEFORE MAXIMUM EFFECT	MAXIMUM EFFECT	DURATION	REACTION	
				DURATION	INTENSITY
I	No effect	No effect	No effect	30 min.	24 mm.
III	No effect	No effect	No effect	None	None
IV	No effect	No effect	No effect	25 min.	16 mm.
V	3 min.	6 mm.	5 min.	None	None
VI	9 min.	8 mm.	20 min.	None	None
VII	2 min.	14 mm.	3 min.	8 min.	10 mm.
VIII	No effect	No effect	No effect	3 min.	8 mm.
IX	No effect	No effect	No effect	6 min.	18 mm.
X	No effect	No effect	No effect	8 min.	12 mm.

Acetylcholine (acecoline) was given in doses of 0.2 gm. subcutaneously but appreciable changes could not be determined in the systolic or diastolic pressures either in the normal or hypertensive subjects. The readings were taken every two minutes for an hour and at short intervals for the next twenty-four hours, but no fall in pressure was observed. This is in marked contrast to the reports of M. Villaret and L. Justin-Besançon[1, 2] who state that the pressure is reduced because of a vasodilator action on the arteries and arterioles. The same authors claim a remarkable effect in arteritis and in senile and diabetic gangrene. The effect of this drug was studied on the central

artery of the retina in normal persons by these authors in collaboration with Schiff-Wertheim[3] and dilatation was observed ophthalmoscopically in 11 of 25 persons examined. It is also stated that no local or general reactions occurred. All of our patients, however, complained of local pain after the injection.

A comparison of the effects of the substances used on the same patient showed that the change after nitroglycerin in our cases of hypertension was inconstant, while amyl nitrite caused a marked fall in every instance. The reduction after amyl nitrite was much greater than after nitroglycerin and the effect lasted almost as long. It is interesting to note that the pressure did not rise to a higher level than originally after amyl nitrite in the control cases, while nitroglycerin often did show such a rise. No change in the blood pressure was noted after acetylcholine, although amyl nitrite and nitroglycerin caused definite reduction in the same patients.

SUMMARY

1. A series of patients with hypertension and renal involvement were given nitroglycerin, amyl nitrite, and acetylcholine after the blood pressure was previously reduced to a fixed level by bed rest, diet, and limitation of fluid intake. The results were controlled by a study of a similar series of normal persons.

2. Nitroglycerin, gr. 1/50, under the tongue produced a fall in blood pressure in all the normal controls, but this effect was inconstant in the patients with hypertension.

3. Amyl nitrite caused a fall in pressure in the controls and hypertensive cases in every instance, being effective also in those instances where nitroglycerin failed to act.

4. A reaction in the form of a temporary rise to a level above that existing before the administration of the drug occurred in a large proportion of the cases with hypertension receiving amyl nitrite or nitroglycerin. The control cases receiving nitroglycerin showed a similar reaction rise, but not those after amyl nitrite. This rise may be of some clinical value in cases of impending or actual cerebral hemorrhage.

5. The effect of amyl nitrite in the doses used was much more marked and lasted almost as long as after nitroglycerin but headache, vertigo, and flushing were more marked after the former drug.

6. Acetylcholine was found to be inert in both the controls and the cases of hypertension, in contradistinction to the claims made in the literature.

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STUDIES ON THE CIRCULATION

II. Cardiac Output in Diseases of the Heart, and Under the Influence of Digitalis Therapy*

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THE circulation of normal human beings can increase in magnitude in response to the greater demands which effort puts upon it. It may increase from three to four times the resting value, and in exceptional cases, as in athletes driven to exhaustion, still more.[1] Analysis of the source of this immense reserve power has led to the conception of the reserve factors in functional sufficiency of the circulation.

Two of these lie in the heart itself, the ventricular output (stroke volume) and ventricular rate. The increase in the rate is the most familiar response to effort and the only one clinically recorded. Its maximal efficient limit is probably not more than twice the resting level. Beyond this increase the efficiency of the heart undoubtedly suffers, because the diastolic interval becomes too short for adequate filling of the heart and for rest for the ventricles.

The ventricular output or stroke volume is clinically rarely estimated and until recently has not been measured at all. Late investigations[2] have shown the magnitude of this factor to depend upon the weight of the subject. It is now well established that the stroke volume divided by the kilograms of body weight is a comparative constant (stroke index) of the average order of 1.5 c.c. That is to say a normal 70 kg. man would have a stroke volume or an output of the heart per beat of about 100 c.c. (70 X 1.5). This stroke index is a useful basis of comparison between the normal and abnormal.

To what extent the stroke volume responds to increased effort has long been debated. It is now clear that in fit and trained subjects it may increase perhaps twofold under severe effort.[3] Under ordinary circumstances in people out of condition this powerful reserve is called on to a lesser degree.

These two factors, stroke volume and ventricular rate, increasing together can under optimal conditions account for a fourfold rise in the minute volume of blood flow (ventricular rate × stroke volume), which is the response of the circulation to the greatest demand that effort puts upon it.

Two other reserve factors, less familiar, are entirely independent of the heart, residing in the blood and muscles of which they are re-

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markable properties. It is necessary to recall the respiratory function of the circulation to make their rôle clear. A greater circulation is needed in exercise in order to remove the increasing quantities of carbon dioxide and to bring fresh supplies of oxygen to restore the lactic acid, produced by muscular contraction, to its precursor. If the circulation for the moment is considered as a means of transporting oxygen from lungs to tissues, it will become clear that since under resting conditions arterial blood gives up only about 25 per cent of its oxygen, a great reserve resides in the possibility of its giving up, let us say, 50 per cent of its oxygen content. In other words the circulation may become twice as effective in its primary function by this means. The difference between the oxygen content of arterial and venous blood will indicate the extent to which this reserve factor is being utilized. It is more convenient to refer to this factor in direct values rather than in percentage. Thus, since the average oxygen content of 100 c.c. of arterial blood is about 20 c.c. and of venous blood about 16 c.c., the difference normally is 4 c.c. An arteriovenous oxygen difference of more than 4 c.c. will, therefore, have the same significance as a rise in pulse rate or stroke volume, that is, to indicate that one of the reserves of the circulation is being called upon. It has been observed that on normal human beings who are not in condition or under special training,[3] the arteriovenous oxygen difference and the ventricular rate are the first reserves of the circulation drawn on under increased effort. Although it is a primary factor in an effective circulation, the arterial oxygen utilization is rarely estimated clinically.

The fourth reserve does not concern us especially, because it is not measurable by the method which we have employed in studying the other reserves. It relates to the ability of muscles to work under an oxygen deficit which the circulation erases after the effort has subsided.

Before we can proceed to the quantitative consideration of these factors in diseases of the heart and vascular system, it is necessary to know the extent to which the circulation is using its reserves under normal conditions. In an earlier publication[4] we gave our experience with the Henderson and Haggard, ethyl iodide method for measuring the circulation in normal human beings. We presented also the data we collected by this means on normal male and female subjects at rest. For the purposes of our present investigation we may adopt the resting values found in this study as normal standards under the conditions and with the method with which we have worked. Our general findings are summarized in Table I.

That is to say, at rest normal human beings receive on the average a discharge of blood to each kilogram of body weight per beat of the heart (stroke index) of 1.5 c.c. Since the total weight determines the total output per beat of the ventricles, a 70 kg. man will have a stroke

TABLE I

DATA ON THE CIRCULATION OF NORMAL SUBJECTS

OBSERVATIONS	WT. KILOGRAMS	ALVEOLAR CO_2 PER CENT	BLOOD FLOW LITERS PER MINUTE	PULSE RATE PER MINUTE	STROKE VOLUME C.C. PER BEAT	STROKE INDEX C.C. PER BEAT—PER KILOGRAM	ARTERIOVENOUS OXYGEN DIFFERENCE C.C. PER 100 C.C. BLOOD
32 Males	68	5.6	8.1	78	102	1.5	3.5
27 Females	58	5.4	7.3	79	93	1.6	3.3

volume therefore of about 100 c.c. By calling on a ventricular rate of from 70 to 80 beats per minute, the circulation achieves a resting minute volume of between 7 and 8 liters. With this volume of blood flow, the tissues need utilize only from 3 to 4 c.c. of oxygen of every 100 c.c. of blood, to cover resting metabolic requirements.

From the clinical standpoint it would be desirable to know how these quantitative factors of the circulation function in heart disease as compared with the normal. Does the range of the reserves become limited? How is the task of maintaining an adequate circulation distributed among them? Is there a difference between mechanical valvular abnormalities and myocardial degeneration? What are the effects of disturbances of rhythm? What happens in heart failure? What is the effect of digitalis therapy?

As a step toward supplying data for an accurate answer to some of these questions, we offer in the present study 340 measurements of the factors of the circulation on 63 patients suffering from a variety of diseases of the cardiovascular system. Resting subjects only were employed, for the obvious reason that most of the cases studied showed far-advanced lesions. About half the cases were in circulatory sufficiency at rest. The others showed clinical symptoms and signs of cardiac insufficiency at rest. The cases have been arranged in ten definitely defined anatomical and etiological groups.

EXPERIMENTAL DATA

1. *Influence of the Pulmonary Factor.*—In measuring the circulation by any method, especially the ethyl iodide method, we really measure the volume flow of blood from right to left heart through the lungs. The accuracy of this method is dependent upon a free exchange of respiratory gases between the alveoli and the pulmonary capillaries. It will be seen that the cases studied presented for the most part advanced lesions. In view of the frequent, inevitable occurrence of congestion of the lungs, sometimes so slight as only to be inferred from symptoms, at other times sufficiently marked to be detected by physical and x-ray signs, it is reasonable to inquire how such a condition or the presence of a hydrothorax affects the value of the data derived. This is not an easy point to investigate with decision on cardiac cases which present other variable factors. It is necessary to use cases with affections of the lungs uncomplicated by heart disease, in which congestive, exudative and sclerotic lesions of different degrees exist. Accordingly we selected a variety of cases of pulmonary tuberculosis in order to test this point.* The findings are recorded in Table II.

It will be seen that the blood flow was constant on the average, irrespective of how much lung was involved. The average minute vol-

*We are greatly indebted to Dr. J. J. Wiener of the division of tuberculosis of the hospital for selecting these cases. Detailed report of this phase of the work will be published elsewhere.

ume was 6.2 liters, and the average weight of these patients was 51 kilograms. Table XIV, in which all our cases are compared on the basis of equal weights, will disclose that these figures compare almost exactly with our normal cases. The lower stroke index (1.2) was due entirely to the more rapid average ventricular rate of the tubercular patients. Moreover, it will be noted that the arteriovenous oxygen difference was also within normal limits. This fact, as we shall later see, is of great significance in demonstrating a circulation that is in normal relation to the metabolism of the subject.

2. *Rheumatic Mitral Stenosis, Regular Rhythm.*—The data on the 6 cases of this group are contained in Table III. So far as we could clinically determine only the mitral valve was involved, but the lesion in each case was anatomically advanced. Cases 1 and 4 were fully compensated, and it is interesting to note that all the factors of the circulation were normal by an ample margin. Cases 2 and 6 had definite symptoms and signs of cardiac insufficiency although not advanced, inasmuch as the patients were capable of leaving their beds on and off. The latter patient improved under rest to a point where the liver receded and moderate activity was resumed. In both cases the stroke index was fixed at the lowest level of normal. That the minute volume was not quite adequate for resting requirements was indicated by the definite increase in the arteriovenous oxygen difference, which is to say that at rest the body was drawing to a considerable extent on a reserve of the circulation ordinarily used only in effort. Patients in Cases 3 and 5 were bedridden with advanced cardiac insufficiency. The factors of the circulation showed a wide quantitative departure from normal standards. There was a marked rise in the ventricular rate, a striking fall in the stroke volume and index and a great increase in the arteriovenous oxygen difference. These findings were typical of clinical cardiac insufficiency, from whatever cause, as we shall presently see.

3. *Rheumatic Mitral Stenosis, Auricular Fibrillation.* 4. *Rheumatic Combined Mitral Stenosis and Aortic Insufficiency, Mitral Stenosis Predominating, Auricular Fibrillation.*—These two groups although clinically separable may, from a functional standpoint, be treated together. The data of the 10 cases are recorded in Tables IV and V. Cardiac insufficiency of varying degrees and chronicity and auricular fibrillation were features of all the cases. They all received digitalis therapeutically or experimentally.

On Cases 10, 11, 12, 13, and 14 there were blood flow determinations before digitalis treatment was begun and during periods when the digitalis was discontinued. It will be noted at once that departures from normal in all the factors of the circulation that characterized cardiac insufficiency in the cases of mitral stenosis with a regular rhythm (Group II) were duplicated in this group. The ventricular

TABLE II

CIRCULATION IN ADVANCED TUBERCULOSIS OF THE LUNGS

NAME	ALVEOLAR CO_2 PER CENT	OXYGEN CONSUMPTION C.C. PER MINUTE	BLOOD FLOW LITERS PER MINUTE	PULSE RATE PER MINUTE	STROKE VOLUME C.C. PER BEAT	STROKE INDEX C.C. PER BEAT PER KG.	ARTERIO-VENOUS OXYGEN DIFFERENCE C.C. PER 100 C.C. BLOOD	REMARKS
A.E.	4.8	299	7.9	119	66	1.2	3.8	Unilateral hydrothorax.
	4.7	307	7.5	122	61	1.1	4.3	
D.L.	5.6	277	5.5	66	83	1.5	5.0	Unilateral pyopneumothorax.
	5.7	223	5.4	70	78	1.4	4.1	
A.H.	4.4	189	5.2	113	46	1.1	3.6	Unilateral pyopneumothorax.
	5.0	187	4.5	105	43	1.0	4.2	
P.N.	5.5	216	7.4	99	75	1.4	2.9	Unilateral hydropneumothorax.
	5.6	198	5.6	91	62	1.1	3.5	
	5.2		6.1	98	64	1.2	3.9	Averages
D.F.	5.5	219	7.4	120	62	1.3	3.0	Advanced tuberculosis of right side. Fibrosis and cavitation. Heart pulled to right.
	5.6	208	4.7	108	44	0.9	4.5	
S.W.	5.8	324	11.0	95	116	2.2	2.9	Extensive tuberculosis of right side. Left lung practically negative.
	5.4	292	7.6	91	84	1.6	3.9	
M.K.	5.3	267	8.0	108	74	1.2	3.3	Predominant infiltration of right side with thickened pleura.
	5.4	265	8.1	105	77	1.3	3.3	
B.G.	4.6	185	6.0	105	57	1.0	3.0	Advanced tuberculosis with fibrosis of right side. Thickened pleura.
	4.8	198	5.0	104	48	0.9	4.0	
S.B.	3.8	217	7.0	122	57	1.2	3.1	Chronic fibrophthisis and cavitation mainly on right side. Bronchiectasis.
	4.6	231	5.9	109	54	1.1	4.0	
E.W.	4.7	197	5.5	119	46	0.9	4.0	Chronic tuberculosis of right side with cavitation. Left slight.
	4.4	208	5.1	126	40	0.7	4.1	
S.G.	4.7	207	5.4	128	42	1.0	3.9	Dense thickened pleura and cavitation on left side. Right negative.
	4.7	214	4.6	121	38	0.9	4.6	
	5.0		6.2	111	60	1.2	3.7	Averages

TABLE II—CONT'D

NAME	ALVEOLAR CO_2 PER CENT	OXYGEN CONSUMPTION C.C. PER MINUTE	BLOOD FLOW LITERS PER MINUTE	PULSE RATE PER MINUTE	STROKE VOLUME C.C. PER BEAT	STROKE INDEX C.C. PER BEAT PER KG.	ARTERIO-VENOUS OXYGEN DIFFERENCE C.C. PER 100 C.C. BLOOD	REMARKS
E.B.	5.4	295	6.6	97	68	0.9	4.5	Bilateral advanced fibroid tuberculosis with emphysema and bronchitis.
	5.7	213	6.6	98	68	0.9	3.2	
B.K.	4.0	274	5.6	104	54	1.2	4.9	Bilateral extensive tuberculosis of all lobes with cavitation.
	3.4	262	5.8	94	62	1.4	4.5	
I.K.	4.4	289	6.2	85	73	1.4	4.7	Bilateral extensive fibrocaseous tuberculosis.
	4.6	237	5.0	79	63	1.2	4.8	
M.L.	4.4	279	7.5	65	114	1.3	3.7	Bilateral extensive tuberculosis. Diffuse nodular infiltrations.
	4.6		8.0	66	120	1.4		
I.N.	5.4	235	5.1	92	57	1.0	4.7	Bilateral fibrocaseous tuberculosis of upper lobes. Cavitation and fibrosis.
	5.4	266	5.3	89	59	1.1	5.0	
A.H.	4.2	221	7.9	109	73	1.1	2.8	Bilateral advanced tuberculosis.
	4.2	334	9.4	104	90	1.4	3.6	
J.D.	4.5	180	9.4	126	75	1.4	1.9	Bilateral extensive tuberculosis.
	3.7	266	8.6	119	72	1.4	3.1	
I.K.	5.4	252	4.2	70	60	1.1	6.0	Bilateral fibrocaseous tuberculosis of upper lobes with emphysema and bronchitis.
	5.4	252	4.1	71	57	1.1	6.2	
D.Y.	4.5	202	4.9	59	83	1.4	4.1	Bilateral fibrocaseous tuberculosis of upper lobes with emphysema and bronchitis.
	4.4	180	4.6	59	78	1.4	3.9	
A.G.	4.8	206	6.0	88	68	1.3	3.4	Bilateral diffuse chronic nodular miliary tuberculosis.
	5.1	217	5.0	80	63	1.2	4.3	
	4.6		6.3	90	73	1.2	4.2	Averages

TABLE III

PURE MITRAL STENOSIS; REGULAR RHYTHM

DATE	NAME	ALVEOLAR CO_2 PER CENT	OXYGEN CONSUMPTION C.C. PER MINUTE	BLOOD FLOW LITERS PER MINUTE	PULSE RATE PER MINUTE	STROKE VOLUME C.C. PER BEAT	STROKE INDEX C.C. PER BEAT PER KG.	ARTERIO-VENOUS OXYGEN DIFFERENCE C.C. PER 100 C.C. BLOOD	REMARKS
6/ 5/28	Case 1	5.1	206	6.9	95	73	2.3	3.0	No digitalis.
	A.W.	5.1	192	6.6	93	71	2.2	2.9	
3/22/28	Case 2	3.4	302	6.0	73	82	1.0	5.0	No digitalis.
	S.K.	3.7	323	6.5	71	91	1.1	5.0	Alveolar CO_2 (Haldane) 3.8%.
5/ 3/28	Case 3	3.8	313	4.6	124	37	0.76	6.8	No digitalis.
	H.A.	3.8	320	3.8	126	31	0.62	8.4	
5/ 5/28		3.8	270	3.8	121	30	0.62	7.4	Alveolar CO_2 (Haldane) 4.0%.
		4.2	266	4.0	122	33	0.66	6.7	
11/ 3/27	Case 4	5.5	176	5.3	104	51	1.8	3.3	Preliminary period.
	M.K.	5.4	129	5.1	101	50	1.7	2.7	
11/10/27		5.6	124	5.3	94	56	1.9	2.4	
		5.7	129	5.4	97	56	1.9	2.3	
				5.3	99	53	1.8	2.7	Averages
12/ 8/27		5.8	205	4.7	97	49	1.7	4.4	Received 6 c.c. tincture digitalis 2 days before in 2 doses.
		5.8	205	4.4	98	44	1.5	4.7	
12/ 9/27		5.6	150	3.4	79	43	1.5	4.4	
		5.4	156	3.7	77	48	1.6	4.3	
				4.0	93	46	1.6	4.4	Averages
1/ 3/28		5.5	135	3.7	90	41	1.4	4.0	Received 18 c.c. tincture digitalis 24 hours before in 4 doses.
		5.5	172	4.0	88	45	1.6	4.3	
1/ 6/28		5.8	140	3.6	73	49	1.7	3.9	
		5.7	134	3.4	79	43	1.5	4.0	
				3.6	83	45	1.5	4.0	Averages
2/ 8/28		5.4	175	3.5	94	37	1.3	5.0	Off digitalis.
		5.5	172	3.9	96	42	1.4	4.4	
2/10/28		5.6	192	3.9	83	47	1.6	4.9	
		5.6	182	3.8	80	41	1.4	5.0	
				3.8	90	42	1.4	4.8	Averages

TABLE III—CONT'D

DATE	NAME	ALVEOLAR CO_2 PER CENT	OXYGEN CONSUMPTION C.C. PER MINUTE	BLOOD FLOW LITERS PER MINUTE	PULSE RATE PER MINUTE	STROKE VOLUME C.C. PER BEAT	STROKE INDEX C.C. PER BEAT PER KG.	ARTERIO-VENOUS OXYGEN DIFFERENCE C.C. PER 100 C.C. BLOOD	REMARKS
2/20/28		5.6	171	4.2	75	56	1.9	4.1	Off digitalis.
		5.5	169	4.3	78	55	1.9	4.0	
2/24/28		5.6	148	4.3	86	50	1.7	3.5	
		5.5	147	4.6	91	51	1.8	3.2	
				4.4	88	53	1.8	3.7	Averages
12/20/27	Case 5 E.S.	3.7	190	2.8	136	20	0.75	7.0	Preliminary period.
		3.7	179	2.4	135	18	0.65	7.5	Alveolar CO_2 (Haldane) 4.0%.
12/22/27		3.6	149	2.2	139	17	0.63	9.1	
		3.6	223	2.5	134	19	0.70	8.8	
				2.5	136	19	0.68	8.1	Averages
1/12/28		3.9	192	2.5	134	19	0.69	7.7	Received 9 c.c. tincture digitalis 2 days before in 3 doses.
1/13/28		4.0	206	2.3	121	19	0.69	7.2	
		4.0	161	2.7	118	20	0.83	7.6	
				2.5	120	20	0.74	7.6	Averages
2/11/28		3.3		2.4	135	18	0.66		Off digitalis.
		3.3	124	1.9	130	15	0.53	6.6	
2/15/28		3.5	162	2.0	127	16	0.60	7.8	
		3.6	170	1.8	130	14	0.50	9.8	
				2.0	131	16	0.58	8.0	Averages
3/22/28	Case 6 M.K.	4.3	242	3.5	73	48	1.1	6.8	Preliminary period.
		4.2	223	4.1	76	54	1.2	5.5	Alveolar CO_2 (Haldane) 4.1%.
3/29/28		4.1	217	4.3	74	57	1.3	5.1	
		4.2	233	4.1	72	57	1.3	5.7	
				4.0	74	54	1.2	5.8	Averages
4/10/28		4.5	245	3.9	69	57	1.3	6.3	Received 12 c.c. tincture digitalis 2 days before.
		4.6	230	4.1	69	60	1.3	5.8	
4/11/28		4.3	270	3.9	78	51	1.1	6.8	
		4.3	271	4.2	77	55	1.2	6.4	
				4.0	73	56	1.2	6.3	Averages

TABLE IV

PURE MITRAL STENOSIS; AURICULAR FIBRILLATION

DATE	NAME	ALVEOLAR CO_2 PER CENT	OXYGEN CONSUMPTION C.C. PER MINUTE	BLOOD FLOW LITERS PER MINUTE	APEX RATE PER MINUTE	STROKE VOLUME C.C. PER BEAT	STROKE INDEX C.C. PER BEAT PER KG.	ARTERIO-VENOUS OXYGEN DIFFERENCE C.C. PER 100 C.C. BLOOD	REMARKS
10/14/27	Case 7 A.E.	3.2	242	3.9	91	42	0.92	6.3	Partially digitalized
4/17/28	Case 8 L.N.	5.0	263	6.0	62	92	1.1	4.4	Fully digitalized
		5.0	258	5.3	65	85	1.0	5.0	
7/20/28	Case 9 M.S.	3.9	290	5.9	91	65	1.1	4.9	p. d.* 9 Partially digitalized
		4.3	214	5.4	88	62	1.1	4.0	p. d. 7
7/21/28		4.1	238	5.7	82	70	1.2	4.2	p. d. 6
		4.4	215	6.2	82	75	1.3	4.0	p. d. 8
12/ 9/27	Case 10 I.J.	4.0	241	4.1	119	34	0.68	6.0	p. d. 15 Preliminary period
12/10/27		3.8	274	3.9	126	31	0.61	7.0	p. d. 14
		4.2	233	3.8	114	34	0.67	6.1	p. d. 14
				3.9	120	33	0.65	6.3	Averages
12/11/27		4.3	239	4.0	100	40	0.79	6.0	p. d. 6 Received 3 c.c. tincture
12/12/27		4.3	218	3.9	89	44	0.89	5.6	p. d. ? digitalis and 2. 5 c.c.
12/14/27		4.1	234	3.7	114	32	0.65	6.4	p. d. ? every day thereafter
12/16/27		4.2	200	3.6	91	39	0.71	5.6	p. d. ?
		4.2	181	3.2	87	36	0.66	5.8	p. d. ?
				3.7	96	38	0.74	5.9	Averages
11/ 3/27	Case 11 J.W.	4.7	211	3.9	117	33	0.98	5.5	p. d. 14 Preliminary period
11/ 8/27		4.7	195	4.0	108	37	1.1	4.9	p. d. 14 Alveolar CO_2 (Haldane)
		4.3	234	3.3	100	33	0.96	7.2	p. d. 12 4.9%
		4.3	190	3.7	104	36	1.1	5.1	p. d. 13
				3.7	107	35	1.03	5.7	Averages
11/16/27		4.6	189	3.7	91	41	1.2	5.1	p. d. 7 Received 7 c.c. tincture
		4.6	184	4.0	94	43	1.3	4.6	p. d. 5 digitalis and 2 c.c. daily
11/18/27		4.9	189	4.3	91	42	1.2	4.4	p. d. 4 for next 18 days
		4.8	190	3.8	90	42	1.2	5.1	p. d. 0
11/25/27		4.9	158	4.3	73	60	1.7	3.7	p. d. 0
		4.9	179	4.2	67	63	1.8	4.4	p. d. 0
12/ 3/27		5.0	174	4.3	65	67	2.0	4.0	p. d. 0

TABLE IV—CONT'D

DATE	NAME	ALVEOLAR CO_2 PER CENT	OXYGEN CONSUMPTION C.C. PER MINUTE	BLOOD FLOW LITERS PER MINUTE	APEX RATE PER MINUTE	STROKE VOLUME C.C. PER BEAT	STROKE INDEX C.C. PER BEAT PER KG.	ARTERIO-VENOUS OXYGEN DIFFERENCE C.C. PER 100 C.C. BLOOD	REMARKS
		4.9	184	4.0	65	62	1.8	4.6	p. d. 0
2/22/28		4.4	206	3.1	100	31	0.91	6.9	p. d. 14 Digitalis discontinued 35
		4.3	216	3.1	94	32	0.95	7.2	p. d. 13 days preceding
2/23/28		4.5	199	3.3	99	33	0.96	6.2	p. d. 13
				3.2	98	32	0.94	6.8	Averages
11/17/27	Case 12	4.8	238	4.6	113	41	1.1	5.2	p. d. 14 Preliminary period
11/21/27	F.M.	5.0	228	4.2	114	37	1.0	5.4	p. d. 13
		5.0	235	4.8	109	44	1.2	4.9	p. d. 13
				4.5	112	41	1.1	5.2	Averages
11/25/27		5.0	225	5.2	101	51	1.4	4.4	p. d. 7 Received 7 c.c. tincture
		5.0	220	5.0	102	49	1.3	4.4	p. d. 5 digitalis day before
11/28/27		4.9	209	4.5	75	47	1.3	4.7	p. d. 4
		5.1	219	4.5	100	45	1.2	4.8	p. d. 4
12/ 1/27		5.0	209	4.1	90	46	1.2	5.1	p. d. 4
		5.1	212	4.7	91	52	1.4	4.5	p. d. 4
				4.7	97	48	1.3	4.7	Averages
2/21/28		4.8	227	4.3	114	38	1.0	5.3	p. d. 17 Digitalis discontinued 23
		5.0	240	4.8	119	40	1.1	5.1	p. d. 15 days preceding
2/22/28		4.8	211	4.8	113	42	1.1	4.4	p. d. 12
				4.6	115	40	1.1	4.9	Averages
3/ 5/28		5.2	224	4.6	89	52	1.4	4.8	p. d. 0 Received 12 c.c. tincture
		5.1	227	4.5	88	50	1.4	5.1	p. d. 0 digitalis day before
3/ 6/28		5.0	198	4.1	78	52	1.4	4.9	p. d. 0
				4.3	85	51	1.4	4.9	Averages
6/21/28		5.1	203	4.9	64	76	2.1	4.2	p. d. 0 Received 2 to 3 c.c. tinc-
		5.1	210	4.9	65	75	2.0	4.3	p. d. 0 ture digitalis daily for
6/26/28		5.0	181	4.4	69	64	1.7	4.2	p. d. 0 preceding 3 months
		5.0	204	5.0	69	72	1.9	4.1	p. d. 0
				4.8	67	72	1.9	4.2	Averages

*Note.—p. d. = pulse deficit.

TABLE V

COMBINED MITRAL STENOSIS AND AORTIC INSUFFICIENCY, MITRAL STENOSIS PREDOMINATING, AURICULAR FIBRILLATION

DATE	NAME	ALVEOLAR CO_2 PER CENT	OXYGEN CONSUMPTION C.C. PER MINUTE	BLOOD FLOW LITERS PER MINUTE	APEX RATE PER MINUTE	STROKE VOLUME C.C. PER BEAT	STROKE INDEX C.C. PER BEAT PER KG.	ARTERIO-VENOUS OXYGEN DIFFERENCE C.C. PER 100 C.C. BLOOD	REMARKS
11/ 4/27	Case 13	3.9	171	3.6	133	27	0.76	4.8	p. d. 11 Preliminary period
11/ 8/27	C. H.	4.0	168	3.6	135	27	0.75	4.8	p. d. 10 Alveolar CO_2 (Haldane)
		3.9	155	3.5	123	29	0.80	4.4	p.d. 10 4.4%
				3.6	130	28	0.77	4.7	Averages
11/16/27		4.4	173	3.3	84	39	1.1	5.2	p. d. 3 Received 12 c.c. tincture
11/17/27		4.6	170	3.6	83	43	1.2	4.7	p. d. 4 digitalis 4 days before
		4.7	170	3.3	85	39	1.1	5.0	p. d. 4 and 1 c.c. daily there-
11/23/27		5.2	201	4.1	104	39	1.1	4.9	p. d. 10 after
		5.0	192	4.0	92	43	1.2	4.8	p. d. 10
				3.7	89	41	1.1	4.9	Averages
1/30/28		4.5	199	3.6	122	29	0.82	5.6	p. d. 9 Digitalis discontinued 13
		4.6	210	3.7	116	32	0.88	5.7	p. d. 9 days preceding
2/ 1/28		4.9	237	3.1	125	25	0.69	7.3	p. d. 10
		4.7	232	3.7	128	29	0.81	6.3	p. d. 10
				3.5	123	29	0.80	6.2	Averages
2/16/28		4.8	170	3.1	79	39	1.1	5.6	p. d. 3 Received 12.5 c.c. tincture
		4.9	163	3.4	79	42	1.2	4.6	p. d. 3 digitalis 5 days before
2/18/28		4.6	206	4.2	88	47	1.3	5.0	p. d. 4 and 1.5 c.c. daily there-
		5.1	202	3.8	90	42	1.2	5.4	p. d. 4 after
				3.6	84	43	1.2	5.2	Averages
6/23/28		4.8	179	4.1	65	63	1.6	4.4	p. d. 0 Received 2 c.c. tincture
		4.9	163	3.6	64	57	1.4	4.5	p. d. 0 digitalis daily for pre-
6/28/28		4.7	173	4.3	70	62	1.5	4.0	p. d. 0 ceding 3 months
		4.8	171	3.9	69	57	1.4	4.4	p. d. 0
				4.0	67	60	1.5	4.3	Averages

TABLE V—CONT'D

DATE	NAME	ALVEOLAR CO_2 PER CENT	OXYGEN CONSUMPTION C.C. PER MINUTE	BLOOD FLOW LITERS PER MINUTE	PULSE RATE PER MINUTE	STROKE VOLUME C.C. PER BEAT	STROKE INDEX C.C. PER BEAT PER KG.	ARTERIO-VENOUS OXYGEN DIFFERENCE C.C. PER 100 C.C. BLOOD	REMARKS	
5/ 4/28	Case 14	5.6	204	3.8	96	40	0.81	5.4	p. d. 4	Preliminary period
	S. G.	5.3	200	4.1	94	43	0.89	4.9	p. d. 4	
				4.0	95	42	0.85	5.2	Averages	
5/ 8/28		5.3	185	4.0	82	48	0.98	4.7	p. d. 0	Received 6 c.c. tincture digitalis 2 days before and 2 c.c. daily thereafter
		5.4	183	3.8	80	46	0.96	4.9	p. d. 0	
				3.9	81	47	0.97	4.8	Averages	
6/20/28		5.5	196	5.0	72	70	1.4	3.9	p. d. 0	Received 2 c.c. tincture digitalis daily for preceding 6 weeks
		5.1	191	4.6	72	63	1.3	4.2	p. d. 0	
7/14/28		5.4	231	5.5	92	60	1.2	4.2	p. d. 0	
		5.3	237	5.0	81	62	1.3	4.8	p. d. 0	
				5.0	79	64	1.3	4.3	Averages	
6/12/28	Case 15	4.1	210	2.8	84	33	0.74	7.6	p. d. 4	Received 2 c.c. tincture digitalis daily for 2 months preceding
6/14/28	R. S.	4.4	204	3.2	60	53	1.2	6.5	p. d. 0	
		4.3	208	2.7	68	40	0.90	7.6	p. d. 0	
8/17/28	Case 16	3.9	282	4.4	80	55	1.1	6.5	p. d. 0	Fully digitalized
	C. D.	3.8	281	5.1	82	62	1.3	5.6	p. d. 0	
8/18/28		3.8	285	4.4	83	53	1.1	6.5	p. d. 0	
		3.6	282	4.4	83	53	1.1	6.5	p. d. 0	
9/14/28		3.5	242	4.2	80	52	1.1	5.8	p. d. 0	
		3.4	279	3.7	73	51	1.1	7.5	p. d. 0	

TABLE VI

PURE AORTIC INSUFFICIENCY; REGULAR RHYTHM

DATE	NAME	ALVEOLAR CO_2 PER CENT	OXYGEN CONSUMPTION C.C. PER MINUTE	BLOOD FLOW LITERS PER MINUTE	PULSE RATE PER MINUTE	STROKE VOLUME C.C. PER BEAT	STROKE INDEX C.C. PER BEAT PER KG.	ARTERIO-VENOUS OXYGEN DIFFERENCE C.C. PER 100 C.C. BLOOD	REMARKS
4/17/28	Case 17	5.8	254	6.3	75	84	1.6	4.0	No digitalis
	M. D.	6.0	252	6.2	71	88	1.7	4.1	
4/13/28	Case 18	4.6	346	8.8	78	114	1.8	4.0	No digitalis
	A. J.	4.0	448	8.8	82	107	1.7	5.1	
12/20/27	Case 19	5.6	184	5.0	118	42	1.4	3.7	Preliminary period
	S. W.	5.7	150	5.6	118	48	1.5	2.7	
		5.6	183	5.5	109	50	1.6	3.4	
12/22/27		5.4	174	6.0	109	55	1.8	2.9	
				5.5	113	49	1.6	3.2	Averages
1/12/28		5.7	182	5.5	114	48	1.6	3.3	Received 11 c.c. tincture digitalis 2 days before
		5.6	193	5.7	112	51	1.6	3.3	
1/13/28		6.0	180	5.5	110	50	1.6	3.4	
				5.6	112	50	1.6	3.3	Averages
2/14/28		5.3	186	4.3	112	38	1.2	4.4	Digitalis discontinued preceding 38 days
		5.2	203	4.9	110	45	1.5	4.1	
2/15/28		5.5	195	4.3	108	39	1.3	4.6	
		5.4	191	5.0	106	47	1.5	3.8	
				4.6	109	42	1.4	4.2	Averages
11/ 2/27	Case 20	5.0	248	5.0	96	52	1.3	5.0	Preliminary period
	J. S.		242	5.5	94	58	1.5	4.4	
11/10/27		4.8	198	5.4	93	58	1.5	3.9	
				5.3	94	56	1.4	4.4	Averages
12/19/27		5.1	213	4.4	80	55	1.4	4.8	Received 14 c.c. tincture digitalis 4 days before
		5.4	233	5.2	86	64	1.6	4.2	
12/21/27		4.9	243	4.5	83	55	1.4	5.3	
		4.8	245	5.2	78	66	1.7	4.8	
				4.8	82	60	1.5	4.8	Averages
1/16/28		4.9	227	5.8	86	68	1.7	3.9	Digitalis discontinued preceding 33 days
		4.8	215	5.2	87	60	1.5	4.1	
1/17/28		4.8	208	4.8	84	57	1.4	4.4	
		5.0	237	5.5	87	63	1.6	4.4	
				5.3	85	62	1.6	4.2	Averages

TABLE VI—CONT'D

DATE	NAME	ALVEOLAR CO_2 PER CENT	OXYGEN CONSUMPTION C.C. PER MINUTE	BLOOD FLOW LITERS PER MINUTE	PULSE RATE PER MINUTE	STROKE VOLUME C.C. PER BEAT	STROKE INDEX C.C. PER BEAT PER KG.	ARTERIO-VENOUS OXYGEN DIFFERENCE C.C. PER 100 C.C. BLOOD	REMARKS
11/ 1/27	Case 21	5.0	259	8.5	96	88	1.8	3.1	Preliminary period
	H. H.	5.0	311	7.6	95	80	1.6	4.1	
11/ 4/27		5.0	323	8.0	96	84	1.7	4.0	
		5.1	289	8.6	92	93	1.9	3.4	
				8.2	95	86	1.8	3.6	Averages
12/ 8/27		5.1	279	6.7	96	70	1.4	4.1	Received 17 c.c. tincture digitalis 2 days before
		5.0	282	6.3	94	67	1.4	4.5	
12/12/27		5.0	317	8.3	111	75	1.5	3.8	
		5.0	254	8.3	111	75	1.5	3.0	
				7.4	103	72	1.5	3.9	Averages
1/ 4/28		4.8	321	6.3	92	69	1.4	5.1	Digitalis discontinued 25 days preceding
		4.8	287	6.6	90	73	1.5	4.4	
1/ 5/28		4.7	254	6.0	88	68	1.4	4.2	
		4.8	297	6.2	91	68	1.4	4.8	
				6.3	90	70	1.4	4.6	Averages
12/ 5/27	Case 22	5.6	225	6.2	69	90	2.4	3.7	Preliminary period
	I. S.	5.5	212	4.9	65	75	2.0	4.4	
12/ 6/27		5.4	224	5.3	62	86	2.3	4.2	
		5.3	180	5.8	61	96	2.5	3.1	
				5.6	64	87	2.3	3.9	Averages
12/16/27		5.5	200	5.4	54	100	2.6	3.7	Received 14 c.c. tincture digitalis 2 days before
12/21/27		5.4	196	5.2	61	86	2.3	3.8	
		5.4	167	5.7	60	95	2.5	2.8	
				5.4	58	93	2.4	3.4	Averages
1/ 4/28		5.7	193	4.7	62	76	2.0	4.1	Digitalis discontinued 21 days preceding
		5.5	202	5.4	60	90	2.4	3.8	
1/ 6/28		5.3	189	5.2	63	82	2.2	3.6	
		5.5	230	4.8	62	78	2.1	4.8	
				5.0	62	81	2.2	4.1	Averages

rates were high, the stroke volumes small. The stroke indices were below 1, and the arteriovenous oxygen differences were above 5. How very markedly abnormal these constant findings were, may be more forcefully gathered from a comparison with the improved findings in those cases which had responded to effective digitalis therapy. The latter values we may assume to have been nearly the normal for these cases (11, 12, 13 and 14).

The other cases (7, 8, 9, 15, 16) were partly or completely under the influence of digitalis when the circulation was originally measured. In spite of the treatment which produced moderate clinical improvement, there were frankly normal findings in none. This is in agreement with the changes in the reserve factors of the circulation that characterize cardiac insufficiency.

In calculating the stroke volume from which the stroke index was derived, we divided the ventricular or apex rate into the minute volume of blood flow. The question arises whether in cases of auricular fibrillation, the apical rate is a measure of the number of effective ventricular strokes. In view of the fact that there is usually a pulse deficit it may be assumed that some of the cardiac contractions do not open the semilunar valves and hence cannot be regarded as producing a ventricular discharge at all. The corrected calculation on the basis of a lower effective ventricular rate (by as much as the pulse deficit) would yield higher and nearer normal values for the stroke volume and index. This point which is of considerable importance, especially in the interpretation of the influence of digitalis therapy, we shall return to later. In the present connection it may be disregarded as immaterial, since in recalculating the stroke volumes on the basis of the radial pulse rates the change in results was less than 9 per cent, still leaving the stroke volumes far from normal.

5. *Rheumatic Aortic Insufficiency, Regular Rhythm.* 6. *Rheumatic Combined Aortic Insufficiency and Mitral Stenosis, Aortic Insufficiency Predominating.*—In Tables VI and VII are recorded the blood flow determinations of these two groups. They were composed of eleven cases, nine of which gave no clinical evidence of cardiac insufficiency. It will be seen that the quantitative factors of the circulation with the exception of the pulse rate were normal or better. In spite of the advanced lesions and the obvious mechanical difficulties under which the heart was laboring, a normal circulation was maintained, adequate for resting requirements. It is interesting to note in this connection that in spite of the left ventricular enlargement, which was a feature of practically all the cases, there was no well-defined increase in the stroke volume.

The blood flow in Case 24 was definitely below normal (low stroke index and elevated arteriovenous oxygen difference). The patient had been decompensated some years before and was moderately insufficient

TABLE VII

COMBINED AORTIC INSUFFICIENCY AND MITRAL STENOSIS AORTIC INSUFFICIENCY PREDOMINATING; REGULAR RHYTHM

DATE	NAME	ALVEOLAR CO_2 PER CENT	OXYGEN CONSUMPTION C.C. PER MINUTE	BLOOD FLOW LITERS PER MINUTE	PULSE RATE PER MINUTE	STROKE VOLUME C.C. PER BEAT	STROKE INDEX C.C. PER BEAT PER KG.	ARTERIO-VENOUS OXYGEN DIFFERENCE C.C. PER 100 C.C. BLOOD	REMARKS
6/ 5/28	Case 23	5.6	227	6.4	92	69	1.5	3.7	No digitalis
	P. G.	5.4	217	5.9	86	69	1.5	3.7	
6/27/28	Case 24	5.2	244	4.7	91	52	1.2	5.1	No digitalis
	Y. L.	5.3	226	4.0	90	44	1.0	5.7	
7/12/28		5.2	200	5.1	102	50	1.2	3.9	
		4.9	221	4.7	102	46	1.1	4.7	
7/19/28	Case 25	5.6	250	6.3	86	74	1.6	4.0	No digitalis
	D. K.	5.4	247	6.1	93	66	1.5	4.0	
7/20/28		5.3	270	6.2	86	72	1.5	4.4	
		5.4	277	5.9	90	66	1.5	4.7	
8/14/28	Case 26	5.1	212	7.0	95	74	1.5	3.0	No digitalis
	H. H.	5.0	235	6.8	84	81	1.7	3.4	
8/16/28		4.9	225	5.8	84	69	1.4	3.9	
		4.9	203	6.1	82	74	1.5	3.4	
8/27/28	Case 27	5.0	344	8.8	69	128	1.6	3.9	No digitalis
	J. P.	5.4	314	8.0	65	124	1.6	3.9	

at the time of the investigation. In Case 26 the patient although able to get about, on and off showed unmistakable evidence of chronic decompensation. His blood flow findings were entirely normal, however. This is one of the two cases in our whole series in which the clinical and laboratory findings are in disagreement.

7. *Rheumatic Combined Aortic Insufficiency and Mitral Stenosis, No Predominance of Either Lesion.*—Of this group of six cases recorded in Table VIII, five were frankly decompensated. Although in Case 28 the patient had a regular rhythm, he improved under rest and digitalis to the point where he was able to get about. His liver receded completely. At the time of the determinations he was still in cardiac insufficiency. But like Case 26 already referred to, he showed normal blood-flow values. Findings in Cases 29, 30, 31, 32 agreed with previous findings in decompensated cases. The latter two, both fibrillators, were fully under the influence of digitalis when examined. The response to the drug was not complete. One was confined to bed, the other was semi-ambulant. Blood-flow measurements reflected this borderline state. There was a reduced stroke volume and an elevated arteriovenous oxygen difference. In Case 33 the patient, who gave no evidence of cardiac failure but suffered from subacute bacterial endocarditis, showed normal blood-flow findings in all respects except the pulse rate.

8. *Hypertension, Cardiac Hypertrophy.*—In this group of 9 cases charted in Table IX our main interest was to determine whether an hypertrophy of the heart uncomplicated by valvular lesions resulted in a greater stroke volume. There were 4 cases of essential hypertension (Cases 35, 36, 42, 43) and 4 cases of hypertension associated with glomerulonephritis (Cases 34, 37, 40, 41). One was a case of unknown etiology. Left ventricular enlargement was a feature of all. Two patients (Cases 34, 41) showed a diminished blood flow similar in magnitude to that found in cardiac insufficiency, although neither had the symptoms and signs of congestive failure. Both patients, however, were in the terminal stages of uremic intoxication, one with a pericarditis and the other ending fatally the following day. Two other patients (Cases 38 and 40) showed evidence of renal insufficiency, but they were both still in good clinical condition. Their blood flow was altogether normal. The other patients, with the exception of Case 42, showed no special clinical features, and the blood flow was within normal limits. In Case 42 the patient was in definite cardiac decompensation with a slow sinus rhythm. Although the stroke volume and index were only at the lower edge of normal, the elevated arteriovenous oxygen difference gave quantitative evidence of the tax on this reserve of the circulation. All factors considered, there seems to be no definite indication of an association of an increased blood flow with cardiac hypertrophy.

TABLE VIII

COMBINED MITRAL STENOSIS AND AORTIC INSUFFICIENCY, NEITHER LESION PREDOMINATING

DATE	NAME	ALVEOLAR CO_2 PER CENT	OXYGEN CONSUMPTION C.C. PER MINUTE	BLOOD FLOW LITERS PER MINUTE	PULSE RATE PER MINUTE	STROKE VOLUME C.C. PER BEAT	STROKE INDEX C.C. PER BEAT PER KG.	ARTERIO-VENOUS OXYGEN DIFFERENCE C.C. PER 100 C.C. BLOOD	REMARKS
12/ 3/27	Case 28	5.2	285	7.7	122	63	1.4	3.7	Preliminary period. Sinus rhythm
	W. L.	5.6	316	8.5	126	67	1.5	3.7	
12/ 5/27		5.2	292	7.8	118	66	1.5	3.8	
		5.6	289	8.2	110	.74	1.8	3.5	
				8.0	119	68	1.6	3.7	Averages
12/14/27		5.4	282	7.5	92	81	1.8	3.8	Received 16 c.c. tincture digitalis
		5.4	262	8.4	85	99	2.2	3.1	day before
12/19/27		5.5	259	7.2	92	78	1.7	3.6	6 days after
		5.5	237	7.0	92	76	1.7	3.4	
1/ 9/28		5.5	265	6.7	100	67	1.5	3.9	25 days after
		5.4	270	6.9	96	72	1.6	3.9	
1/16/28		5.4	280	7.0	92	72	1.6	4.0	32 days after
4/ 6/28	Case 29	5.1	229	3.9	94	42	0.82	5.8	No digitalis
	S. J.	5.1	253	4.1	90	45	0.89	6.2	
1/27/28	Case 30	4.9	192	4.0	82	49	1.1	4.8	No digitalis
	R. R.								
7/18/28	Case 31	4.9	290	4.9	88	57	1.1	5.9	Received 2 c.c. tincture digitalis
	H. Z.	5.1	261	4.6	76	60	1.2	5.7	daily for 2 months
7/27/28		5.4	251	4.4	68	64	1.2	5.8	Auricular fibrillation
		5.0	257	3.7	66	56	1.1	6.9	
7/21/28	Case 32	3.7	247	4.8	88	54	1.0	5.2	Fully digitalized
	S. S.	3.7	222	4.7	82	57	1.1	4.8	Auricular fibrillation
7/23/28		4.9	254	4.8	84	58	1.1	5.2	
		4.9	240	4.3	71	60	1.1	5.6	
8/27/28	Case 33	4.7	229	8.2	104	79	1.6	2.8	Subacute bacterial endocarditis
	P. A.	4.8	227	8.2	105	78	1.6	2.8	

TABLE IX

HYPERTENSION; CARDIAC HYPERTROPHY

DATE	NAME	ALVEOLAR CO_2 PER CENT	OXYGEN CONSUMPTION C.C. PER MINUTE	BLOOD FLOW LITERS PER MINUTE	PULSE RATE PER MINUTE	STROKE VOLUME C.C. PER BEAT	STROKE INDEX C.C. PER BEAT PER KG.	ARTERIO-VENOUS OXYGEN DIFFERENCE C.C. PER 100 C.C. BLOOD	REMARKS
4/ 4/28	Case 34 Y. W.	4.8	144	4.5	120	37	0.86	3.2	Azotemia. Pericarditis. Uremia
1/11/28	Case 35	5.8	269	7.8	108	72	1.2	3.5	
	M. H.	5.4	222	6.4	97	66	1.1	3.5	
6/ 1/27	Case 36 B. B.	5.0	271	6.8	82	84	1.1	4.0	
5/20/27	Case 38	4.9	202	10.1	90	112	2.1	2.0	Azotemia. Pericarditis. Uremia
	R. L.	4.8	209	8.5	87	99	1.9	2.5	
3/30/27	Case 39	5.3	268	9.6	71	135	1.8	2.8	
	M. G.	5.1	240	8.6	71	120	1.6	2.8	
2/17/28	Case 40	4.9	219	6.5	77	85	1.4	3.3	Azotemia. Renal insufficiency
	R. B.	4.8	216	6.3	72	88	1.4	3.4	
3/ 2/28		5.2	249	6.3	71	89	1.4	3.9	
1/28/28	Case 41,	4.5	265	3.6	107	33	0.56	7.4	Azotemia. Uremia. Died following day
	S. G.	4.5	267	3.6	102	35	0.59	7.5	
1/19/28	Case 42	4.1	282	5.7	74	77	1.1	5.0	
	J. R.	4.1	254	6.0	59	100	1.5	4.3	
4/11/28		5.2	366	5.6	72	77	1.1	6.6	
		5.4	245	4.9	60	81	1.2	5.0	
5/17/27	Case 43 L. P.	5.7	239	10.1	102	99	1.5	2.4	

TABLE X

ARTERIOSCLEROTIC HEART DISEASE; HEART-BLOCK

DATE	NAME	ALVEOLAR CO_2 PER CENT	OXYGEN CONSUMPTION C.C. PER MINUTE	BLOOD FLOW LITERS PER MINUTE	PULSE RATE PER MINUTE	STROKE VOLUME C.C. PER BEAT	STROKE INDEX C.C. PER BEAT PER KG.	ARTERIO-VENOUS OXYGEN DIFFERENCE C.C. PER 100 C.C. BLOOD	REMARKS
4/18/28	Case 44 W. S.	4.1	368	4.7	97	48	0.67	7.8	
		4.0	259	5.0	90	56	0.77	5.1	
3/29/27	Case 45 M. B.	5.3	234	5.3	69	77	1.3	4.4	
7/16/28	Case 46 L. R.	5.4	275	6.5	95	68	1.2	4.3	Fully digitalized. Sinus rhythm
		5.2	239	6.5	95	68	1.2	4.0	
7/17/28		5.4	291	6.6	94	70	1.2	4.4	
		5.7	282	6.7	91	75	1.3	4.3	
9/ 5/28		4.5	325	4.9	109	45	0.78	6.6	Off digitalis for 48 days
		4.6	287	4.7	104	45	0.78	6.6	
5/10/27	Case 47 H. S.	5.1	298	11.5	98	118	1.4	2.6	Preliminary period. Auricular fibrillation
5/11/27		5.3	290	9.4	95	99	1.2	2.3	
5/13/27		5.4	340	8.7	82	106	1.2	3.9	Received 15 c.c. tincture digitalis
5/16/27		5.3	175	7.6	75	102	1.2	2.3	
5/18/27		5.1	207	7.4	65	116	1.3	2.8	
10/13/27		5.4	324	8.0	80	100	1.1	4.0	1 c.c. digitalis daily for months
10/14/27		5.5	324	6.9	76	91	1.0	4.7	
10/18/27		5.3	300	7.8	84	93	1.0	3.9	
10/12/27	Case 48 D. L.	5.1	253	4.6	130	36	0.55	5.6	Preliminary period. Auricular fibrillation
		5.0	250	4.2	128	33	0.51	6.0	
10/17/27		5.0	155	3.3	104	32	0.51	4.8	Received 21 c.c. tincture digitalis in past 48 hours
10/18/27		5.0	164	4.5	96	47	0.73	3.7	
10/19/27		5.2	202	3.5	92	37	0.58	5.9	
2/21/26	Case 61 H. L.	6.0	178	3.6	44	82	2.1	5.0	Complete heart-block
		6.0	203	3.9	45	86	2.2	5.2	
3/30/26	Case 62 I. A.	3.8	320	5.2	28	188	2.7	6.1	Complete heart-block Auricular fibrillation
2/25/26	Case 63 M. L.	5.2	221	5.9	40	146	2.6	3.8	Complete heart-block

TABLE XI

SYPHILITIC HEART DISEASE; ANEURYSM; CONGENITAL HEART DISEASE; MISCELLANEOUS CONDITIONS

DATE	NAME	ALVEOLAR CO_2 PER CENT	OXYGEN CONSUMPTION C.C. PER MINUTE	BLOOD FLOW LITERS PER MINUTE	PULSE RATE PER MINUTE	STROKE VOLUME C.C. PER BEAT	STROKE INDEX C.C. PER BEAT PER KG.	ARTERIO-VENOUS OXYGEN DIFFERENCE C.C. PER 100 C.C. BLOOD	REMARKS
4/20/28	Case 49	4.9	239	5.4	75	71	1.4	4.5	Syphilitic aortitis with aneurysm
	N. R.	4.8	205	5.0	72	69	1.3	4.1	
5/ 3/28		4.6	228	5.1	74	68	1.3	4.5	
		4.8	218	5.0	72	69	1.3	4.4	
7/26/28	Case 50	4.9	312	7.9	85	94	1.4	4.0	Syphilitic aortitis with aneurysm and aortic insufficiency
	J. Y.	5.0	266	7.2	80	90	1.4	3.7	
7/27/28		5.2	295	7.6	78	98	1.5	3.9	
		5.0	285	7.9	77	102	1.6	3.6	
7/23/28	Case 51	5.0	274	5.8	89	65	1.4	4.7	Syphilitic aortitis with aneurysm
	A. K.	5.1	255	5.0	80	62	1.3	5.1	
4/20/28	Case 52	4.2	272	5.0	103	48	1.2	5.5	Congenital heart defect
	L. W.	4.0	282	4.5	97	46	1.1	6.3	Pulmonic stenosis
5/ 2/28		4.3	182	4.0	91	44	1.1	4.5	
		4.0	218	3.8	88	43	1.1	5.9	
4/24/28	Case 53	3.3	220	3.8	98	39	0.97	5.8	Congenital heart defect
	D. P.	3.3	191	3.5	90	38	0.96	5.6	Pulmonic stenosis
11/23/26	Case 54 R. S.	3.2	216	3.1	105	30	0.70	7.0	? Congenital heart defect

TABLE XI—CONT'D

DATE	NAME	ALVEOLAR CO_2 PER CENT	OXYGEN CONSUMPTION C.C. PER MINUTE	BLOOD FLOW LITERS PER MINUTE	PULSE RATE PER MINUTE	STROKE VOLUME C.C. PER BEAT	STROKE INDEX C.C. PER BEAT PER KG.	ARTERIO-VENOUS OXYGEN DIFFERENCE C.C. PER 100 C.C. BLOOD	REMARKS
1/28/27	Case 55	5.4	249	7.6	89	85	1.5	3.3	Congenital heart defect
	F. B.	5.5	221	6.6	83	79	1.4	3.4	Patent ductus arteriosus
10/17/26	Case 56	4.7	213	4.7	86	55	1.5	4.5	Congenital heart defect
	M. H.			4.8	80	60	1.6	4.5	Patent ductus arteriosus
10/20/26		4.7	212	5.5	80	69	1.8	3.8	
12/29/27	Case 57	4.2	306	5.4	97	56	0.82	5.6	Tuberculous pericarditis
	M. G.	4.2	328	5.6	98	57	0.83	5.8	Cardiac insufficiency
3/29/28	Case 58	4.7	419	7.1	121	58	0.95	5.9	Graves' disease
	S. M.	4.8	385	7.4	132	56	0.92	5.2	
3/31/28		5.3	362	7.7	120	65	1.06	4.7	
		4.9	405	7.4	125	59	0.97	5.5	
	Case 59 K. S.	4.2	194	4.7	94	50	1.23	4.1	Primary anemia
5/11/28	Case 60	5.4	313	7.8	103	75	0.91	4.0	Secondary anemia
	L. A.	5.5	320	8.0	102	79	0.95	4.0	
5/12/28		5.4	320	7.8	101	77	0.93	4.1	
		5.2	305	8.2	100	82	0.99	3.7	

9. *Arteriosclerotic Heart Disease. Heart-block.*—In this group charted in Table X we had 5 cases showing various lesions of arteriosclerotic heart disease and 3 cases of heart-block presumably on the same basis. In cases 44, 45, 46 the patients showed electrocardiographic evidence of myocardial degeneration. In Case 45 the patient had a sinus rhythm and no symptoms of cardiac failure. He showed a practically normal blood flow. In Case 44, patient also had a sinus rhythm but was definitely decompensated. His blood flow showed all the features characteristic of this condition. Case 46 was similar to the latter but in addition the heart was fibrillating. When fully digitalized, his blood flow was within normal limits, but when experimentally taken off digitalis his pulse rate rose, the stroke volume and index declined markedly and the arteriovenous oxygen difference increased beyond normal. In short, he presented the typical quantitative features of cardiac failure. Patient 47 had fibrillation and chronic decompensation. She had been partly under digitalis when she arrived at the hospital, where she was under observation for over six months. During this period she was kept more or less fully digitalized. Under these conditions the blood flow figures were found to be at the lower level of normal. Case 48 showed rapid auricular fibrillation. The patient did not respond to digitalis and succumbed some months later. He too showed widely abnormal measurements of the circulation typical of a failing heart.

Patients 61, 62, 63, suffered from heart-block with complete dissociation. None showed clinical signs of cardiac insufficiency and all were ambulant. The chief quantitative finding was the strikingly increased stroke volume and index. This was the only type of case that showed this feature in our whole series.

10. *Syphilitic Heart Disease. Aneurysm. Congenital Heart Disease. Miscellaneous Conditions Affecting the Heart.*—The data on these miscellaneous cases are charted in Table XI. Patients 49, 50, 51 had definite symptoms and x-ray evidence of aneurysm. Aortic insufficiency was also present in Patient 50. Although the lesions were anatomically advanced in all three, the circulation was perfectly sufficient. The reserve factors of the circulation were all within normal limits by an ample margin.

There were 5 cases in this group classed as congenital hearts. Patients 52 and 53 were very definitely such from the signs, x-ray findings and clinical courses. Although not suffering from congestive failure strictly speaking, they presented marked symptoms as a result of their pulmonic artery stenosis. The former was complicated by tuberculosis. The pulse was raised, the stroke index was below normal, and the arteriovenous oxygen difference was markedly elevated. The diagnosis in Case 54 was debatable as to the congenital origin. There were

TABLE XII

SUMMARY OF EFFECT OF DIGITALIS ON CASES WITH SINUS RHYTHM

CASE NO.	TYPE	BLOOD FLOW LITERS PER MINUTE	PULSE RATE PER MINUTE	STROKE VOLUME C.C. PER BEAT	STROKE INDEX C.C. PER BEAT PER KG.	ARTERIOVENOUS OXYGEN DIFFERENCE C.C. PER 100 C.C. BLOOD	REMARKS
4	Mitral stenosis	4.5	92	49	1.7	3.7	No digitalis
		3.8	88	46	1.6	4.2	Digitalized for short period. No effect
5	Mitral stenosis	2.3	133	18	0.63	8.0	No digitalis
		2.5	120	20	0.74	7.6	Digitalized for short period. No effect
6	Mitral stenosis	4.0	74	54	1.2	5.8	No digitalis
		4.0	73	56	1.2	6.3	Digitalized for short period. No effect
19	Aortic insufficiency	5.0	111	46	1.5	3.7	No digitalis
		5.6	112	50	1.6	3.3	Digitalized for short period. No effect
20	Aortic insufficiency	5.3	90	59	1.5	4.3	No digitalis
		4.8	82	60	1.5	4.8	Digitalized for short period. No effect
21	Aortic insufficiency	7.3	93	77	1.6	4.1	No digitalis
		7.4	103	72	1.5	3.9	Digitalized for short period. No effect
22	Aortic insufficiency	5.3	63	83	2.3	4.0	No digitalis
		5.4	58	93	2.4	3.4	Digitalized for short period. Doubtful effect
28	Mitral stenosis. Aortic insufficiency	7.5	107	69	1.6	3.8	No digitalis
		7.5	90	85	1.9	3.5	Digitalized for short period. Doubtful effect
46	Arteriosclerotic heart disease	4.8	106	45	0.78	6.6	No digitalis
		6.6	94	70	1.2	4.3	Digitalized for long period. Marked effect

clear signs of congestive failure, however, and the measurements of the circulation were in agreement with this state. Patients 55 and 56, without symptoms and in good health, probably had patent ductus arteriosus. The circulation in both was perfectly normal.

The remaining 4 cases were of mixed varieties. Case 57 was one of active tuberculosis with congestive heart failure resulting from advanced tuberculous adhesive pericarditis. The factors of the circulation were affected in a manner characteristic of heart failure.

Case 58 was one of advanced Graves' disease. The metabolism was much elevated during the determinations, from plus 50 to 85 per cent. This increased oxygen consumption was not met with an increased blood flow, but rather by a greater utilization of arterial oxygen. The stroke volume was below normal; and although it seems more reasonable to interpret it as a result of the tachycardia rather than of an essential decline in cardiac output, it nevertheless indicates poor heart action. As Henderson[3] has shown, an increased demand on the circulation is met in healthy subjects by a steady or increasing stroke volume in spite of the rapid rate.

Two cases of anemia, one primary (Case 59) and one secondary (Case 60), showed no notable features.

11. *Influence of Digitalis Therapy.*—How digitalis brings about improvement in heart failure is still uncertain. Graphic methods have given conclusive data on the action of the drug on the conductive system. Hence, where advantageous changes in rate and rhythm are factors in improvement, the rôle of digitalis is understood. But largely for lack of methods of direct investigation, the action of digitalis is still obscure in those cases where its use is beneficial without primarily affecting the rate or rhythm.

Clinical writers have long adopted the idea that digitalis increases the output of the heart and explained its favorable action in heart failure by assuming a restoration of a diminished blood flow to normal levels. Recent studies by means of x-ray and blood-flow measurements have thrown doubt on this attractive conception. Harrison and Leonard[7] have found in short experiments that digitalis decreases the blood flow in normal dogs. Burwell, Neighbors and Regen[8] report similar findings in normal human beings. Cohn and Stewart[9] have shown too that the early action of digitalis results in a diminished output of the heart but that this effect is later overcome by the greater contraction of the heart muscle when an increased blood flow follows.

From the measurements we have made on the quantitative factors of the circulation in our cases of heart disease, we may analyze the action of digitalis more directly than has hitherto been possible under clinical conditions. Twenty-three cases of our series received digitalis experimentally or as part of their treatment in the wards. Of these, nine had

a sinus rhythm and fourteen were cases with auricular fibrillation. In Tables XII and XIII we have summarized the data given in full in the earlier tables.

Unless otherwise stated the cases were rapidly digitalized with body-weight doses of the tincture of digitalis (1.5 minims per pound). When no more than this quantity was given, it is referred to in the tables as "digitalized short period." When the administration of digitalis was continued in maintenance doses after the initial rapid digitalization, it is referred to as "digitalized long period." Those cases that received less than body-weight doses are referred to as "partially digitalized."

In none of our cases of chronic rheumatic cardiovalvular disease with a sinus rhythm was the administration of digitalis accompanied by any clinical improvement. In Cases 4, 5, 19, 21, in which electrocardiograms were taken, the T-waves promptly became negative in two or more leads, indicating that the drug was actively absorbed.

In agreement with the clinical observations reference to Table XII reveals no definite or consistent change in the quantitative factors of the circulation as a result of the administration of digitalis. With the possible exception of a variable tendency to reduce the pulse rate slightly, the influence of digitalization in Cases 4, 5, 6, 19, 20, 21, was not detectable. Of this series Case 5 only was decompensated. Although there was some increase in the stroke volume as a result of the reduction in pulse rates in both Cases 22 and 28, we must regard these as exaggerated day-to-day variations in cases of aortic insufficiency with unusually large stroke volumes, rather than a significant digitalis effect. This view is supported by the absence of electrocardiographic evidence of digitalis action in both cases.

The only one in our series of subjects with sinus rhythm which was definitely influenced by digitalis was Case 46. The patient was markedly decompensated, on admission, with dyspnea, edema, a large liver, and gave electrocardiographic evidence of myocardial degeneration. He improved under digitalis therapy and diuretics. The blood flow at this time was well within normal limits except for a pulse rate of 94. Digitalis was experimentally withdrawn, and the symptoms of heart failure returned. The pulse rate and arteriovenous oxygen difference rose, and the minute volume, stroke volume, and stroke index fell to levels characteristic of cardiac decompensation. Whether this finding is exceptional or characteristic of the action of digitalis in decompensated cases of arteriosclerotic heart disease with sinus rhythm, we are not in a position to say.

The improvement of cases with auricular fibrillation under the action of digitalis is a common clinical experience. Whether this is brought about through the effect of the drug on the restoration of a normal rate, or an increase in the stroke volume, or both, has never

TABLE XIII

SUMMARY OF EFFECT OF DIGITALIS ON CASES WITH AURICULAR FIBRILLATION

CASE NO.	TYPE	BLOOD FLOW LITERS PER MINUTE	APICAL RATE PER MINUTE	RADIAL RATE PER MINUTE	STROKE VOLUME C.C. PER BEAT (APICAL)	STROKE VOLUME C.C. PER BEAT (RADIAL)	STROKE INDEX C.C. PER BEAT PER KG. (APICAL)	STROKE INDEX C.C. PER BEAT PER KG. (RADIAL)	ARTERIO-VENOUS OXYGEN DIFFERENCE C.C. PER 100 C.C. BLOOD	REMARKS
7	Mitral stenosis. Marked decompensation	3.9	91		42		0.92		6.3	Partially digitalized. Slight effect
8	Mitral stenosis. Moder. decompensation	5.6	63		87		1.1		4.7	Fully digitalized. Definite effect
9	Mitral stenosis. Moder. decompensation	5.8	86	79	68	74	1.2	1.3	4.3	Partially digitalized. Definite effect
10	Mitral stenosis. Marked decompensation	3.9 3.7	120 96	106 90	33 38	37 41	0.65 0.74	0.73 0.82	6.3 5.9	No digitalis Digitalized short period. Slight effect
11	Mitral stenosis. Moder. decompensation	3.5 4.0 4.2	103 92 65	90 88 65	34 42 65	39 45 65	0.98 1.20 1.9	1.1 1.3 1.9	6.3 4.8 4.3	No digitalis Digitalized short period Digitalized long period. Marked effect
12	Mitral stenosis. Marked decompensation	4.5 4.7 4.8	114 97 67	100 93 67	41 48 72	45 50 72	1.1 1.3 1.9	1.2 1.4 1.9	5.1 4.7 4.2	No digitalis Digitalized short period Digitalized long period. Marked effect
13	Mitral stenosis and aortic insufficiency. Marked decompensation	3.6 3.7 4.0	126 89 67	116 83 67	29 41 60	32 44 60	0.79 1.1 1.5	0.88 1.2 1.5	5.4 4.9 4.3	No digitalis Digitalized short period Digitalized long period. Marked effect

TABLE XIII—CONT'D

CASE NO.	TYPE	BLOOD FLOW LITERS PER MINUTE	APICAL RATE PER MINUTE	RADIAL RATE PER MINUTE	STROKE VOLUME C.C. PER BEAT (APICAL)	STROKE VOLUME C.C. PER BEAT (RADIAL)	STROKE INDEX C.C. PER BEAT PER KG. (APICAL)	STROKE INDEX C.C. PER BEAT PER KG. (RADIAL)	ARTERIO-VENOUS OXYGEN DIFFERENCE C.C. PER 100 C.C. BLOOD	REMARKS
14	Mitral stenosis and aortic insufficiency. Marked decompensation	4.0 3.9 5.0	95 81 79	91 81 79	42 47 64	44 47 64	0.85 0.97 1.3	0.90 0.97 1.3	5.2 4.8 4.3	No digitalis Digitalized short period Digitalized long period. Marked effect
15	Mitral stenosis and aortic insufficiency. Marked decompensation	2.9	64		47		1.1		7.0	Digitalized long period. Definite effect
16	Mitral stenosis and aortic insufficiency. Moder. decompensation	4.5	80		54		1.1		6.4	Digitalized long period. Definite effect
31	Mitral stenosis and aortic insufficiency. Marked decompensation	4.4	74		59		1.2		6.0	Digitalized long period. Definite effect
32	Mitral stenosis and aortic insufficiency. Moder. decompensation	4.6	81		57		1.1		5.2	Digitalized long period. Definite effect
47	Arteriosclerotic. Moder. decompensation	10.4 7.9 7.9	97 74 80		109 108 95		1.3 1.2 1.0		2.5 3.0 4.2	Partially digitalized Digitalized short period Digitalized long period. Diminished effect.
48	Arteriosclerotic. Moder. decompensation	4.3 3.8	129 97		35 39		0.53 0.58		5.8 4.8	No digitalis Digitalized short period. No effect

been demonstrated. Our investigation supplies some data on this point. Cases 11, 12, 13, 14 (Tables IV and V) showed great clinical benefit from prolonged digitalis therapy. The period before digitalis treatment was begun and the period after digitalis was discontinued have been averaged under the identification of "no digitalis" (Table XIII). It will be seen that the measurements of the "no digitalis" period were all abnormal, of the type associated with heart failure. That is, the ventricular rate was high with a large pulse deficit, the stroke volume and stroke index were below the normal range, and the arteriovenous oxygen difference was much elevated.*

The effect of a short period of digitalization was moderate although very definite and consistent. The heart rate was brought down and the pulse deficit reduced; the stroke volume and index were increased; and the arterial oxygen utilization was lowered. After prolonged digitalis therapy, these factors became completely normal showing a total improvement from 50 to 100 per cent.

It must be emphasized that the increase in the minute volume, although definite, was smaller and not in proportion to the change in heart rate and stroke volume. The significance of this will be considered later.

The other cases in our series of auricular fibrillation (Table XIII) support the general findings of the better controlled cases already discussed. Patients in Cases 7 and 10 were very ill (the latter died in the hospital). Both showed but slight clinical improvement on digitalis, and the lack of response was apparent also in the insignificant quantitative changes in the measurement of the circulation. In Cases 8, 9, 15, 16, 31 and 32 we had no determinations before digitalis was given. In spite of the absence of this control it was possible to deduce a definite effect resulting from the administration of digitalis similar in type if not quite the same in magnitude to the controlled Cases 11, 12, 13 and 14. They were of the same clinical types as the latter and responded to treatment in much the same way although not so satisfactorily. A reason for this might be found in the advanced age of this group which averaged over thirty-five years, and hence these patients having suffered from the disease longer may have had less responsive hearts. The significant point, however, remains that the figures for pulse rate, stroke volume and stroke index were very much nearer normal than we had reason to expect them to be if these cases had remained untreated with digitalis. Comparison of these figures with those of untreated cases who were equally decompensated will bring this point out (Cases 3, 11, 12, 13, 14, 29, 46, 48, 57).

*It will be noticed that calculating the stroke volume on the basis of the effective beats (radial rate), the stroke volumes and indexes of these cases although somewhat higher were still definitely abnormal. It cannot be argued that the improvement in these two items which followed the administration of digitalis was only apparent and due to the action of the drug in eliminating the ineffectual beats of the heart as factors in the calculation, since on the corrected basis the improvement was just as striking.

Of the two cases of arteriosclerotic heart disease with fibrillation only one responded satisfactorily. Patient Case 48 was very ill and received no benefit from digitalization. His blood flow showed this too. He died shortly thereafter in the hospital. Case 47 was kept comfortable under digitalis, and her blood flow figures were in agreement with this state.

TABLE XIV

SUMMARY OF QUANTITATIVE FINDINGS IN CASES OF HEART DISEASE COMPARED ON BASIS OF SIMILAR AVERAGE WEIGHTS*

CASES	AVERAGE WEIGHT KILOS	BLOOD FLOW LITERS PER MINUTE	PULSE RATE PER MINUTE	STROKE VOLUME C.C. PER BEAT	STROKE INDEX C.C. PER BEAT PER KILO.	ARTERIO-VENOUS OXYGEN DIFFERENCE C.C. PER 100 C.C. BLOOD
31 Normal cases	64 *49*	7.7 *6.0*	79 79	98 *76*	1.55 1.55	3.4 3.4
51 Cases of compensated cardiac disease	55 *49*	5.8 *5.5*	81 81	72 *68*	1.40 1.40	4.2 4.2
17 Cases of decompensated cardiac disease	49	4.0	108	38	0.78	6.0
12 Cases of decompensated cardiac disease improved by digitalis	53 *49*	5.0 *4.8*	75 75	67 *64*	1.3 1.3	4.9 4.9

*For derivation, see text.

Summary of Quantitative Findings.—In Table XIV we have averaged the results on all our compensated and decompensated cases and compared them with averages on our normal series previously published. In order to make the figures truly comparable it is necessary to deal with subjects that are of about the same weight, since the stroke volume is a function of the weight. Our series of patients included a considerable number of children. Moreover most of the others were in a state of undernutrition so that the average weight proved to be below the normal. We have, therefore, calculated what we might expect the stroke and minute volumes to have been, from the stroke index and ventricular rate experimentally found, employing the lowest average weight of our three large groups as the basis, that is the 49 kilograms of the decompensated cases. Thus if the average weight of the normal group was 49 kilograms, the stroke volume would be 76 c.c. (49 × 1.55 the stroke index), and the minute volume would be 6 liters (76 × 79 the ventricular rate). Similarly in the group of compensated cases, the stroke volume would be 68 c.c. (49 × 1.4), and the minute volume would be 5.5 liters (68 × 81). These figures appear in italics in Table XIV.

If our cases are divided into three broad groups, a significant comparison becomes at once clear. Those cases of heart disease classed as compensated varied so little from the normal as to warrant no quanti-

tative distinction. The cases classed as decompensated, on clinical grounds, showed a wide quantitative difference from the normal. The minute volume was 30 per cent below the normal, the pulse rate was elevated by 30 beats per minute, the stroke volume was half the normal as was also the stroke index, and the arterial oxygen utilization was almost doubled. The cases that were effectively digitalized, by clinical criteria, showed values that had strikingly returned to nearly normal levels. These changes have a related significance which we may now discuss.

DISCUSSION

This study attempts to contribute to the accumulation of the kind of quantitative data upon which an explanation of the dynamics of cardiac disorders may ultimately be based. Although the necessary data are being gathered from several sources,[9, 10, 11] the sum is still small and too untried from a critical point of view, to warrant extensive interpretations. We cannot, therefore, at this time do more than emphasize what appear to be acceptable facts and indicate the general meaning.

In tracing the physiological implications of our data, it must not be understood that we are offering an explanation of the clinical conditions under discussion, but rather *a picture of what constitutes these conditions in quantitative terms.* Those who, in attempting to corrolate anatomical and clinical findings, have had the common experience of discovering perfectly good heart muscles at the post-mortem table in patients who have died of heart failure, will appreciate the need for distinguishing between the fact and the explanation.

Moreover, it is well to bear in mind the limitation of this study. *We are concerned only with resting subjects.* The circulation is a function with a wide range in responding to normal conditions. In many respects this is its most important quantitative feature. How this range is affected by diseases of the heart is not in the sphere of this study, since our patients could not easily be subjected to the test of effort. The clinical symptoms of dyspnea, fatigability and pain of the compensated cases clearly point, however, to a marked influence in the direction of a contraction of the range of the circulation. With the method of investigation which we have used we get no clue of a departure from normal magnitudes until the heart action has been restricted by disease to the point where it is insufficient for the resting state. This point, it will be recognized, is identical with the clinical condition of heart failure. Hence, when our data disclosed, as we have seen, that the quantitative factors of the circulation were changed only in cardiac insufficiency, it need not be concluded that a decline in these factors did not exist before the phenomena of heart failure appeared. If the circulation had been measured under conditions of effort in the

compensated cases of heart disease, no doubt similar changes might have been brought out. It is possible too perhaps to bring out in this way quantitative differences between the anatomical varieties of heart disease, in which respect our data failed to give any evidence.

The Minute Volume.—The volume of blood flowing from the heart into the arterial system, as has been said, can be resolved into the two factors of the stroke volume and the heart rate. The essentially passive rôle of the left side of the heart in controlling the volume output is commonly lost sight of. It can eject less, but no more, blood than the right heart sends it. The right heart in turn expels a volume of blood determined by the volume of the venous return. What factor fixes the level of the venous return is not definitely known; although there is ground for belief that it is probably more closely related to the need for disposing of carbon dioxide produced, than for the supply of oxygen (since returning venous blood still holds a large reserve of available oxygen). We may be content with the general statement that the metabolic activity is in some manner the determining factor in the volume of venous return. Adopting the accepted practice of expressing metabolic activity by the oxygen consumption, a definite normal relation can be said to exist between the oxygen consumption and the venous return and hence the minute volume of blood flow.

A quantitative expression of this normal relation can be derived from the arteriovenous oxygen difference, which we have seen discloses that from every 100 c.c. of blood flowing from the heart a relatively constant quantity of oxygen is taken away by the tissues under normal resting conditions. It is derived by dividing the minute volume of blood flow stated in deciliters, into the c.c. of oxygen consumed per minute.

Our normal cases (Table XIV) show an average of 3.4 c.c. If we accept 4 c.c. as an average upper normal limit, the relation of the resting oxygen consumption to the resting minute volume of blood flow per unit of time may be expressed in this general way,

$$\frac{O}{V} = 4$$

where O is the oxygen consumption in c.c. per minute, and V is the minute volume of blood flow in deciliters.

It will be readily admitted that whatever the state of health of the circulatory apparatus, metabolism goes on. The resting oxygen consumption cannot diminish. O, therefore, may be regarded as constant, and whatever variations in the quotient $\frac{O}{V}$ appear in heart disease must therefore be attributable to a change in the variable V. The possibility of an increase in V seems remote, for with a constant oxygen consumption there is no stimulus for a larger venous return than obtains normally. As long as the heart action is capable of handling

the venous return called forth by the unchanged oxygen consumption, V will remain undiminished and the quotient $\frac{O}{V}$ will stay at 4. On the other hand, the possibility for a decline in V is strong. If the heart action as a result of disease is not equal to the task of advancing the venous return to the arterial side, V must decline and the quotient $\frac{O}{V}$ will rise above 4. In such an event there must be an accumulation of blood on the venous side, a condition which will clinically be expressed by the phenomena of congestive failure. The degree to which the heart fails in advancing the venous return will be expressed by the degree of rise in the quotient $\frac{O}{V}$.

It is significant, therefore, that in our cases of cardiovascular disease classed as compensated, that is having no clinical evidence of congestive failure, the arteriovenous oxygen difference or $\frac{O}{V}$ quotient was found to be 4.2, a difference from the normal so small that no significance can be attached to it. This means that the minute volume was in practically normal relation to the oxygen consumption, or again that the venous return was completely advanced to the arterial side, and hence there was no accumulation of blood on the venous side. In other words, since the minute volume found (Table XIV) was 5.5 liters, we may assume that the venous return was of this order.

On the other hand, in our cases of cardiovascular disease classed as decompensated, that is having abundant clinical evidence of congestive failure, the arteriovenous oxygen difference or $\frac{O}{V}$ quotient was found to be 6. This means that the minute volume was not in normal relation to the oxygen consumption, or again that the minute volume was less than the venous return, and hence there was a detectable accumulation of blood on the venous side. In point of fact the minute volume (Table XIV) was found to be 4 liters as compared with a probable venous return of the order of 5.5 liters.

Stroke Volume.—In accounting for the failure of the heart to advance the venous return completely to the arterial side, it is necessary to examine the components of the minute volume. We have already seen that the latter is the product of the ventricular rate and the stroke volume, that is to say

$$V = R \times S$$

where R is the ventricular rate and S is the stroke volume.

It follows, therefore, that R and S are inversely related to each other. That is to say, with a constant V, if the rate rises the stroke volume must decline, and if the rate declines the stroke volume must increase. Evidence of the latter we have already encountered in our

cases of heart-block, which showed a very large stroke volume as a result of the low ventricular rate (Table X). The former relation is common even in normal beings[3] when the rate rises through toxic agencies such as tobacco, atropine or mental excitement without physical effort. This dependence of the size of the stroke volume on the rate must necessarily be so, since a more rapid rate will shorten diastole and ventricular relaxation, which in consequence diminishes ventricular filling. This effect will, moreover, be accentuated in cases of mitral stenosis (to which class most of our cases of cardiac insufficiency belonged) on account of the mechanical obstruction to ventricular filling.

This inverse relationship between R and S somewhat complicates the interpretation of changes in the stroke volume S. As long as V remains constant, a decline in S may be attributed to a rise in R. But if V declines along with S, an essential decrease in the stroke volume S must be admitted. And on the other hand, if V remains unchanged, an increase in S may be attributed to a reduction in R, but if V increases along with S, an essential increase in the stroke volume S must be admitted beyond the influence of R.

In Table XIV it will be seen that the average S of our decompensated cases was 38 c.c. This stroke volume was half the output in our normal series and practically half the output in our cases without cardiac insufficiency. We may ask, therefore, whether the markedly diminished stroke volume of 38 c.c. was real or the result of the tachycardia, for in these cases a rapid ventricular rate averaging 30 beats per minute above the normal rate was an almost invariable feature. For, an essential or real diminution in the stroke volume would account for the failure of the heart in these cases to advance the normal venous return to the arterial side, or in other words for the failure of the heart to produce a normal minute volume.

Even allowing for the rapid rate in our cases, an actual decline in the stroke volume must be admitted. It will be seen that the minute volume averaged 4 liters, whereas in the compensated cases it was 5.5 liters and in the normal cases 6 liters. In other words, V decreased along with S, and an essential diminution in the stroke volume in heart failure must, therefore, be a fact. How much of an actual decline there was we can only estimate, but it was certainly not as great as the 50 per cent found.

The significance of the tachycardia is not easy to determine. In the majority of our cases of heart failure auricular fibrillation was a feature, and the elevated R may be attributed to the accident of a disturbed rhythm. On the other hand many cases of cardiac insufficiency with a sinus rhythm show a rapid rate also. It is possible in these cases that the ventricles are not able to accept the burden thrown on them by a slow pulse and that the tachycardia is a necessary compen-

sating effect. It would be interesting to note whether slowing the rate in this type of case by other means than digitalis is well borne.

Digitalis.—If the primary feature of heart failure consists in a diminished stroke volume, we may inquire whether digitalis affects the clinical improvement in these cases through a restoration of a normal stroke volume. We are unable to answer this important question at present with certainty. The interpretation of the data on our cases is still debatable, because the number of cases in which we have well-controlled preliminary periods is small, and we are forced to consider an average effect of digitalis rather than the effect in individual cases. We are reinvestigating this question on a more extended scale and under more guarded conditions.

In only one instance (Case 46), strangely enough with a sinus rhythm, was the increase in stroke volume so large as to be beyond any question of the influence of the slowing in R. In this case V increased along with S by almost 40 per cent.

In Table XIV the effect of digitalis is averaged on twelve cases that had responded with partial or complete clinical improvement. It will be seen the R had been slowed to 75 beats per minute and that S increased to 64 c.c. In spite of the fact that the ventricular rate was even slower than in our normal and compensated heart cases, the stroke volume did not quite reach the S in these cases. The failure of digitalis to bring the stroke volume completely back to normal is not essential, however, to an admission that there was probably a real increase in this factor, since the average includes cases that were only partially improved clinically. Moreover, there was a definite rise in V from the low level found in heart failure, that is the minute volume increased from 4 liters to 4.8 liters, and as we have seen when both V and S increase, the latter is more than an effect of the slower rate. But was the increase in V sufficiently large to be significant?

The average arteriovenous oxygen difference or $\frac{O}{V}$ quotient in the treated cases, including those digitalized with partial and complete effect, was 4.9 as compared to 6 for the untreated cases. The decline in the quotient toward a normal level can be accounted for only by a significant increase in V, since O, the resting oxygen consumption, cannot be considered to have changed. This deduction supports the significance of the rise in the minute volume from 4 liters in the undigitalized cases to 4.8 liters in the treated cases. Incidentally it may be pointed out that the falling $\frac{O}{V}$ quotient also indicates that the heart was advancing the venous return more completely to the arterial side. This perhaps accounts for the resolution of the phenomena of congestive failure under digitalis therapy.

In the 4 cases that were controlled with measurements of the circulation before digitalis was begun (Cases 11, 12, 13, and 14, Table XIII)

the clinical improvement was very marked. The digitalis effect can be said to have been complete, since the rate was brought down into the sixties. Whereas the stroke volumes increased from 50 to 100 per cent above the untreated levels, the minute volumes were only moderately increased. A significant interpretation becomes difficult. It is impossible to say with conviction that in these 4 cases, our best controlled, the rise in S was significantly beyond the influence of the reduction in R, since V did not increase sufficiently along with S.

In view of these incomplete findings we must postpone a decision as to whether digitalis achieves its clinical benefit from a slowing of the ventricular rate alone or also through an essential increase in the stroke volume.

If digitalis does not restore the minute volume to normal, its effectiveness resolves itself mainly into a shifting of the burden of maintaining an unaugmented minute volume from one cardiac reserve to another, that is from an increased ventricular rate and a low stroke volume, to a slow rate and an increased stroke volume. Although it is difficult to see how the phenomena of congestive failure can be resolved under these conditions alone, the change is not without beneficial clinical consequences. To begin with, from the standpoint of the circulation, a normal minute volume is not absolutely essential, for it can continue to draw on an increased oxygen utilization to discharge its respiratory function completely. This fact is often lost sight of. The circulation even in cardiac failure is performing its function completely but at great effort and expense to its reserves. It cannot be overemphasized that the ventricles are first of all muscles, in whose effective operation rest is the most essential element. As the rate is reduced under digitalis, an improvement in muscular activity of the heart may in time take place. It is quite possible that since whatever increase in stroke volume we found appeared after prolonged digitalis therapy, such improvement was the result of the prolonged rest given to the heart through this undisputed action of digitalis.

The vulnerability of a circulation maintained at the expense of a rapid rate and a high arterial oxygen utilization, although performing its respiratory function completely, must be stressed. For any of the indispensable and ordinary efforts of life, such as turning in bed, taking meals, straining or nervous excitement must tax the reserves to still greater limits. When we consider that the stroke volume has already failed and the ventricular rate and the arterial oxygen utilization are exploited to the limits of efficiency, it becomes clear how full of hazard a circulation achieved at such expense must be. The already weakened ventricles are driven to the limit without proper interval for rest. A reduction of the rate is, therefore, the most immediate agent of relief; and if digitalis does nothing more than that, it accomplishes a great deal. It is putting the heart itself to bed.

SUMMARY AND CONCLUSIONS

The conception of the stroke volume, ventricular rate, and arterial oxygen utilization as reserve factors in the circulation which may be drawn on in effort, is outlined. The extent to which these three reserves contribute to the circulation in normal resting subjects is reviewed.

Data derived from 340 measurements of the circulation on 63 cases of a variety of cardiovascular diseases, by means of the Henderson and Haggard ethyl iodide method is presented.

The influence of pulmonary disorders, such as congestion or hydrothorax, on measurements of the circulation is discussed. From an analysis of measurements of the circulation in 21 cases of pulmonary tuberculosis, it was found that disorders of the lungs did not affect the measurement of the circulation.

Irrespective of the anatomical or etiological variety, the resting minute volume, ventricular rate, stroke volume and arterial oxygen utilization were not significantly different from the normal in cardiovascular diseases without cardiac insufficiency. There was a possible exception to this conclusion in cases of congenital heart disease with pulmonic artery stenosis.

Cases suffering from cardiac insufficiency as judged by clinical criteria, of whatever anatomical or etiological origin, showed a diminished minute volume, an accelerated ventricular rate, a diminished stroke volume and an increased arterial oxygen utilization. A circulation of sufficient magnitude to carry on the internal respiratory function was, however, maintained by the increased use of the two reserves of ventricular rate and arterial oxygen utilization.

Cardiac enlargement, as judged by clinical criteria, was not associated with an increased stroke volume.

In three cases of heart-block there was a markedly increased stroke volume.

The influence of digitalis on 23 cases is described. In 9 cases with a sinus rhythm no beneficial effect on the reserve factors of the circulation was detected, with the single exception of a case of arteriosclerotic heart disease with cardiac insufficiency. In 14 cases with auricular fibrillation and cardiac insufficiency, digitalis restored the ventricular rate and stroke volume to almost normal values, but produced improvement in the minute volume and arterial oxygen utilization to lesser degrees.

The significance of these findings in relation to the dynamics of heart failure and the therapeutic action of digitalis is discussed.

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DISPLACEMENT OF THE LEFT NIPPLE IN MITRAL STENOSIS*

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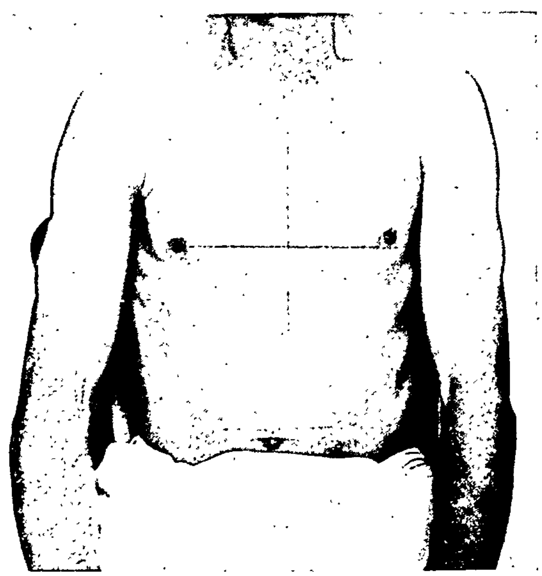
DEFORMITY of the chest in the precordial region, in the absence of disease of the bony thorax is commonly seen in patients with organic heart disease. Indeed, at one time minute mensuration of the chest was practiced with a view of arriving at a diagnosis of valvular heart disease.[1] A correlation of the actual lesions of the heart with such changes in the shape of the chest, however, has never been attempted.



Upward and outward displacement of the left nipple in a man thirty-three years old with mitral stenosis, in whom there were no auscultatory signs of any valvular lesion and in whom fluoroscopic examination revealed a very small heart. The electrocardiogram showed right ventricular predominance with notched P-waves in all three leads.

I have recently been impressed with a deformity in the contour of the chest which seems specific for mitral stenosis. It is the upward and outward displacement of the left nipple which obviously is seen only in children and male adults.

In a group of 200 healthy adult males, I have found the left nipple displaced outwardly in only one individual who had had rickets in early childhood.

In a series of 200 consecutive patients with frank mitral stenosis, 130 adult males and 70 children, varying in age from four to seventy years, I have found this sign positive in over 90 per cent of the cases.

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Of course I have omitted examining any patients with pendulous breasts.

In some of these cases in addition to the outward displacement, I have noted the left nipple to be different from the right in size, shape, and color. In several instances the left nipple was much smaller than the right, the areola was lighter in color and ovoid in contour instead of round.

The following explanation of this phenomenon may be attempted:

With the enlargement of the heart and the increased intra-auricular pressure that takes place as a result of stenosis or damage to the mitral valve, the left auricle dilates and encroaches upon the retrocardiac space. As this chamber dilates, it causes the right ventricle to be pushed forward close to the ventral surface of the anterior chest wall. If the patient is so young that the costosternal junctions are not yet fixed, then the continual pounding of the right ventricle against the anterior chest causes bulging of the cartilage and bones overlying it. A resulting deformity takes place in the region of the mesial left half of the sternum and the adjacent second, third, and fourth costosternal junctions. One severe bout of rheumatic fever in childhood when the chest is still yielding is sufficient to produce this deformity.

The displacement of the left nipple takes place as a result of the adjustment of the muscles and fascia overlying the bulging precordium.

I have not observed this sign in 9 patients with isolated aortic insufficiency or in 10 cases of congenital heart disease.

SUMMARY

In healthy children and in male adults both nipples are usually on the same level. In patients with mitral disease of the heart, who have had rheumatic fever in childhood, the dynamics of the valvular lesion cause a deformity of the chest in the region of the left half of the sternum and the adjacent second, third, and fourth costosternal junctions. Because of this there results an upward and outward displacement of the left nipple. This sign is not present in patients with isolated aortic insufficiency or congenital heart disease. It was present in over 90 per cent of 200 consecutive patients with mitral stenosis examined at the Montefiore Hospital within the last two years.

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MONOPHASIC AND DEFORMED VENTRICULAR COMPLEXES RESULTING FROM SURFACE APPLICATIONS OF POTASSIUM SALTS*

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THE occurrence of monophasic ventricular complexes or of deflections in which the descending limb of R is extended by a rounded hump or merges into a declining plateau has been demonstrated both experimentally and clinically in connection with coronary occlusion followed by infarction. They have been suspected also in association with myocarditis due to rheumatic fever (Cohn and Swift,[1] Porte and Pardee[2]) and have been demonstrated to occur in association with pericarditis and hemopericardium by Katz, Feil and Scott.[3]

While studying the effects of potassium ions upon the intact dog's heart it was found that the intrapericardial injection or localized application of concentrated KCl solutions produced electrocardiograms of a similar nature. The records reproduced as Figs. 1, 2 and 3 are presented as examples of the successive changes found in Lead II. They were recorded by a Victor electrocardiograph arranged to record on a laboratory photokymograph, together with a time record.

Experiment 0-73.—Segment A of Fig. 1 is a control. A 20 per cent KCl solution was applied on the apex of the left ventricle by means of a camel's-hair brush, and Segment B was at once recorded. Segment C was recorded one minute later. Another application was made and three minutes thereafter the curves of Segment D were registered. The heart surface was thoroughly washed with normal saline and three and a half minutes later the record shown in Segment E was taken.

Experiment 0-74.—Segment A of Fig. 2 is a control. B and C were taken one-fourth and one minute respectively after application of 20 per cent KCl solution on several areas of the right ventricle. A further application was made and curves of Segment D were obtained. The curves of Segment E were obtained eight minutes later without wasting the heart.

Experiment 0-70.—Segment A of Fig. 3 is a control. Segment B shows the effect of injecting 4 c.c. of 5 per cent KCl solution into the intact pericardial sac. In addition to characteristic deformation of the ventricular complexes, sinus slowing obtains one minute thereafter. Segment C shows the effects two minutes after injection. After recovery from these effects, the auricle was stimulated by artificial induc-

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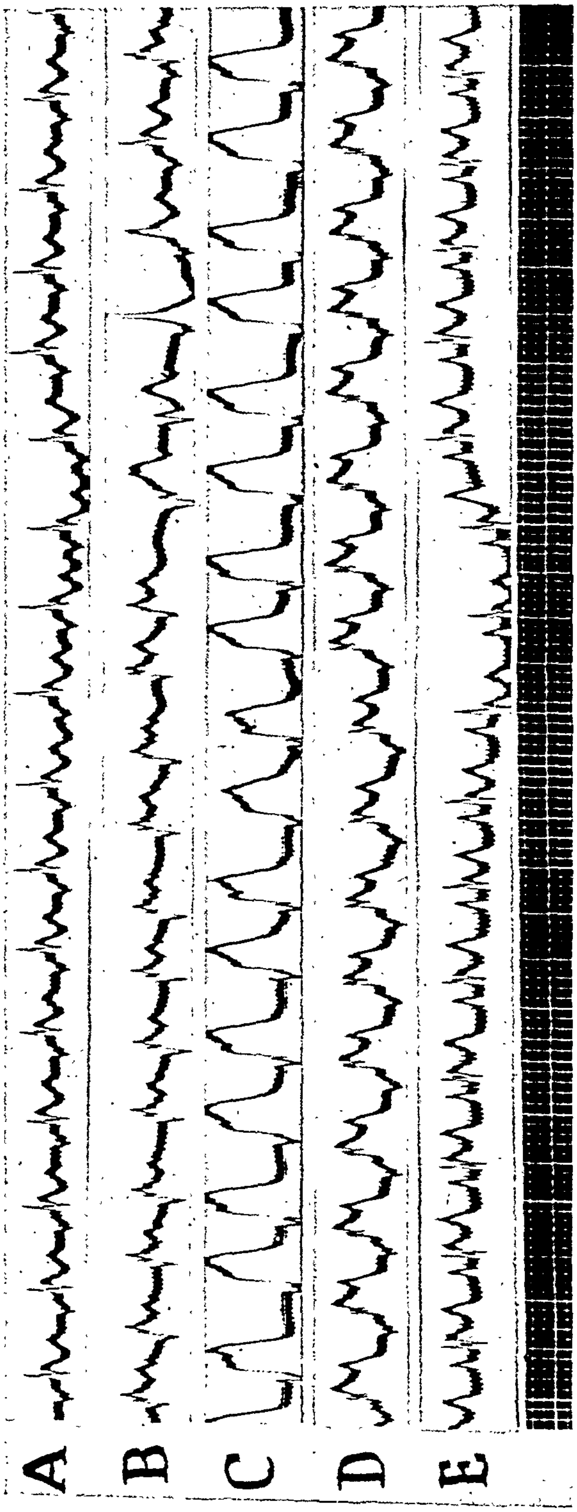

Fig. 1.

tion shocks just discernible as sharp deflections preceding the P-wave in Segment D, which is also a control. Three c.c. of 5 per cent KCl solution was again introduced into the pericardial sac. Records in Segments E and F were taken fifteen seconds and two and three-quarter minutes later. The typical change in the ventricular complexes without change in rate are well shown. The pericardial cavity was washed with saline, and two minutes thereafter the last segment was recorded.

The records require no further discussion, as they speak for themselves.

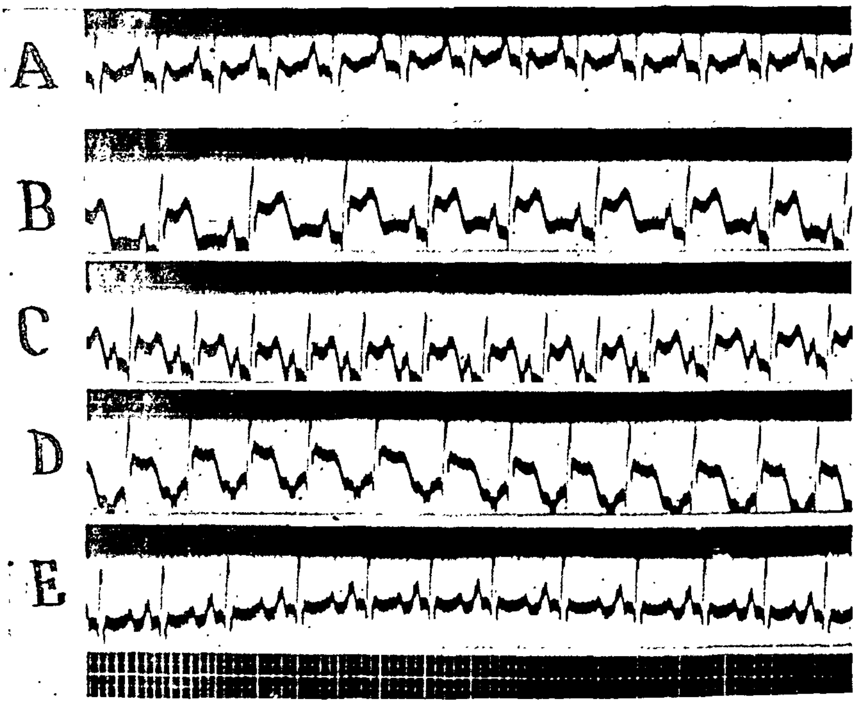

Fig. 2.

The importance of these observations is threefold: First, the fact that chemicals, like potassium, which depress conduction, are capable of producing changes in the electrocardiographic complexes similar to those following coronary obstruction should lead clinicians to temper any diagnosis of coronary disease on the basis of electrocardiographic changes alone. Several other conditions causing depressed conduction may produce ventricular complexes of similar form.

Second, these observations supply the first crucial demonstration that chemicals introduced into the pericardial sac or applied to the surface of the mammalian ventricles are capable of affecting the ventricular beat directly. In 1915, Gunn and Martin[4] professed to have demonstrated such an action, but an examination of their experiments with pilocarpine, adrenalin, etc., by the critical reader will show that

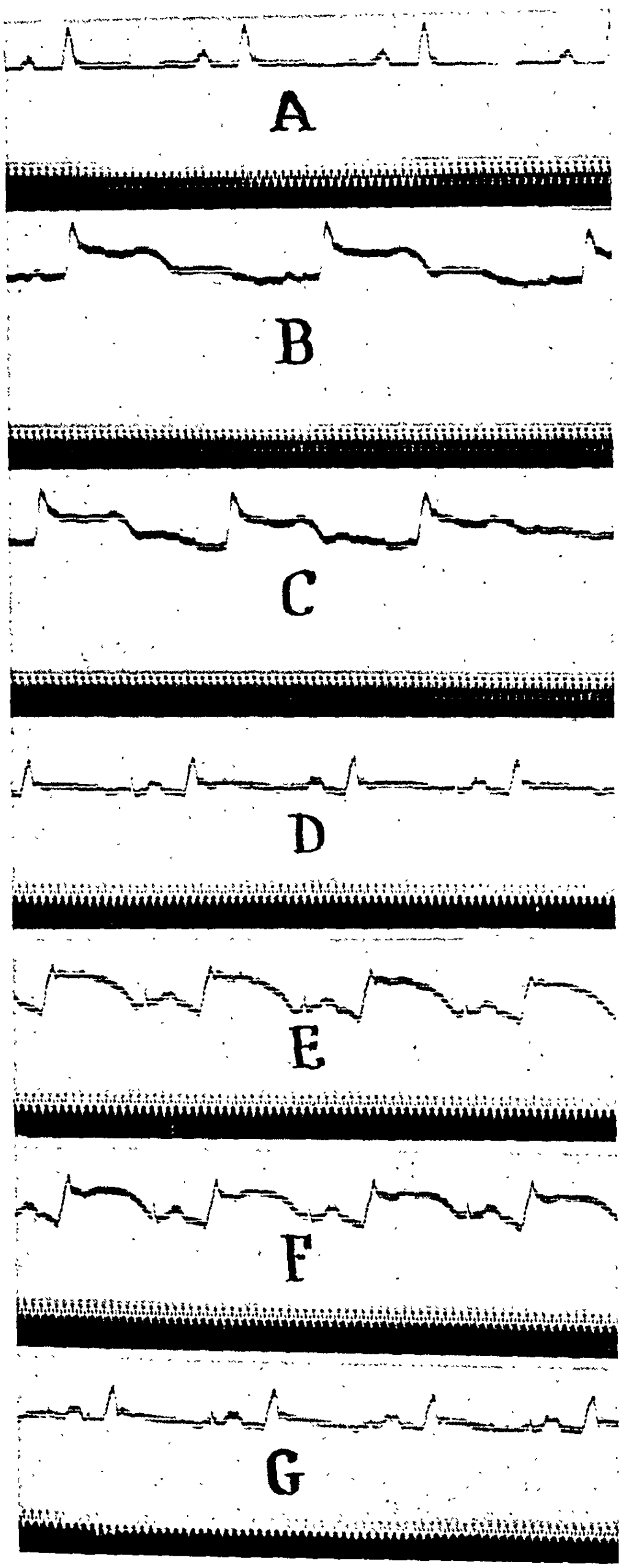

Fig. 3.

they demonstrated only effects produced through auricular absorption and contain no proof that the ventricles were affected otherwise than through secondary changes in rate.

Third, the unsuspected fact that chemical substances are so easily absorbed from the epicardial surfaces is of great clinical interest. It not only opens up therapeutic possibilities but also gives an explanation as to why toxins formed by virulent organisms within the pericardium prove so serious for the ventricle.

SUMMARY

1. It was demonstrated that concentrated KCl solutions applied to the ventricular surfaces or injected into the pericardial sac in small quantities produce either monophasic or deformed ventricular complexes resembling those due to coronary occlusion.

2. Since similar changes in the form of ventricular complexes occur as a result of this and other conditions, caution in the interpretation of such waves is urged.

3. The observations represent the first crucial proof that drugs and chemicals can be directly absorbed from the ventricular surface in mammalian hearts.

4. The therapeutic possibilities are suggested.

5. A logical explanation for the rapid cardiac depression which follows virulent forms of pericarditis is given by these results.

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STUDIES OF VENTRICULAR FIBRILLATION CAUSED BY ELECTRIC SHOCK

II. Cinematographic and Electrocardiographic Observations of the Natural Process in the Dog's Heart. Its Inhibition by Potassium and the Revival of Coordinated Beats by Calcium*†

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(In Collaboration With James R. Bell, M.D., and Margaret Paine)

INTRODUCTION

RECENTLY we[1] reported experiments on the revival of the dog's heart from ventricular fibrillation. Briefly summarized, it was shown that ventricular fibrillation produced by faradic stimulation can be abolished by intracardiac injection of a 5 per cent KCl solution in doses of 1 c.c. per kilogram. Massage was not required in order to produce these effects, but injections into both ventricular cavities appeared to be essential for prompt action. After every trace of fibrillation had disappeared, a subsequent injection into both ventricular chambers of a 5 per cent $CaCl_2$ and 0.1 per cent heparin solution restored a coordinated beat, only, however, when supplemented by cardiac massage.

This paper is chiefly concerned with detailed studies of the fibrillary process, the alterations effected by potassium before complete inhibition occurred, and the mechanisms concerned in revival. Aside from their purely scientific interest, these and subsidiary problems are of practical importance as well, because the basic changes involved in the cardiac mechanism supply scientific proof that the reported resuscitations could by no chance have been a matter of fortunate spontaneous revival.

THE LIMITATIONS AND POSSIBILITIES OF GRAPHIC METHODS APPLIED TO FIBRILLATING VENTRICLES

The hopelessness of following the incoordinate movements over individual portions of the ventricle by inspection has led investigators to adopt myocardiographic and electrocardiographic methods in their study. But the older mechanical methods were often employed without their inadequacy being realized, and the interpretations of electrocardiograms have not always been tempered with the necessary caution.

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†Published by the Physiology Committee on Electric Shock.

In our investigations on ventricular fibrillation, we endeavored to employ the newer aids in graphic registration; hence it was important to orient as to the significance of results that may be obtained by their use.

Accurate mechanical registration of the fibrillating ventricles has proved impossible in the past because efficient and responsive apparatus could not be built. Now that the difficulties in the construction of adequate mechanical recorders have largely been overcome, we are still confronted with the quandary that any mechanical appliance, no matter how efficient or whether it takes the form of surface myograph, cardiometer or intraventricular pressure recorder, constitutes an instrument which records not the ultimate contractions of the ventricle but the resultants of many simultaneous phenomena occurring in successive intervals of time. Our understanding of the intimate nature of ventricular fibrillation has undoubtedly been impeded by our inability to fathom what is taking place in these ultimate fractions of cardiac muscle. The difficulty exists to a certain extent even when the heart is beating in a coordinate manner. Thus, one of us[2] has recently pointed out that intraventricular pressure curves can be used as graphic evidence as to what the ultimate fractions are doing only because their sequence and orderliness cannot easily be changed under physiological experimental conditions. When, as apparently occurs in fibrillation, the excitation is irregular, disordered and unpredictable from moment to moment, intraventricular pressure curves give no direct evidence as to the character of the fibrillary process. Their value in understanding the mechanisms of fibrillation is only indirect in nature. We may illustrate our meaning by an actual observation: The intraventricular pressure curves of Fig. 1 show that after induction of fibrillation the intraventricular pressure curves alter to a remarkable degree. The pressures which normally varied between 5 and 100 mm. Hg with each cardiac cycle suddenly fall to a mean value of about 10 or 20 mm. Hg. The large, regular, characteristic pressure pulses are replaced by very small, uneven, irregular undulations which bear no direct relation to the fibrillary movements or, as in this instance, by no variations at all.

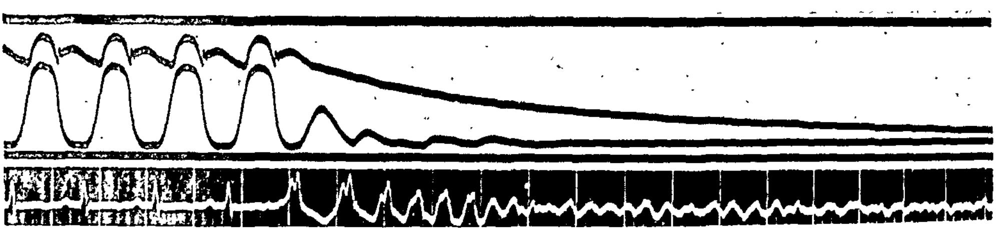

Fig. 1.—Aortic and left ventricular pressure curves and electrocardiogram (Lead II) showing the effects introducing ventricular fibrillation due to faradic excitation. 1 to 2—Initial tachysystole stage. 2 to 3—Stage of consecutive incoordination. Time 0.04 and 0.2 sec.

While it is clear that intraventricular pressure records cannot be

employed to interpret the variations in the strength and frequency of fractionate ventricular contractions, they are of service in another direction. They demonstrate that fibrillation which follows faradic stimulation rapidly passes into such a degree of incoordination that any semblance of regular pressure curves ceases within a second after applying a faradic current. As far as the pressure curves are concerned, the preliminary stage in which a state of tachysystole can be said to exist is extremely short.

Volume curves of the ventricles are of less value than inspection. They show an immediate increase in the size of the heart with the onset of fibrillation, an increase which progresses as fibrillation continues. Inspection gives the same evidence of dilatation but shows in addition that it is due to the predominate dilatation of the right ventricle. Indeed as fibrillation continues, the ballooning effect due to returning blood becomes so extreme on the right side that the left ventricle may have the appearance of a small rounded tumor protruding from the right ventricle. Such an increase in size has frequently been misinterpreted as evidence of an atonic condition of ventricular muscle or of a state equivalent to paralysis. As already pointed out, pressure curves from the left as well as from the right ventricle show that for a long time a pressure range from 10-20 mm. Hg. persists, a finding inconsistent with the idea of atonia. Myographic records from the left ventricle give additional evidence that the mean effect of the fibrillating contraction is to hold ventricular musculature in a position approximately midway between that of systole and diastole. In the right ventricle, however, the venous blood which is pumped into the right ventricle by the continued contractions of the right auricle soon develops sufficient pressure to overcome the tendency to diminish the size of the right ventricle. Moreover, myographic appliances attached to the surface of the heart give no direct evidence as to the character or rate of fibrillary contractions occurring in the ventricle unless they are attached in great numbers and are applied so as to record contractions between points not more than 2 or 3 mm. apart.

With the introduction of the electrocardiograph for practical use, it was generally believed that it offered a method far superior to any mechanical appliance for studying the ultimate character of the fibrillary process. Convenient as the procedure has become, it is not without drawbacks both in its application and in the interpretation of the graphs. When the records are derived by one of the customary three leads, it should be kept in mind that the electrocardiographic oscillations correspond in neither amplitude, regularity nor frequency to the ultimate contractions occurring in any portion of the ventricle. Like the normal electrocardiogram deflections, they represent the first differential quotient of the algebraic sum of potential differences that occur in the heart from moment to moment, oriented in the direction

of the lead. There are these added difficulties in the case of fibrillating ventricles, namely, (1) that the plane of orientation is continually changing as the heart progressively dilates, and (2) that the amplitude and frequency of electrocardiographic deflections due essentially to excitation may not correspond in magnitude or number to the sums of fractionate contractions simultaneously operating in the ventricles.

Studies by Means of Moving Pictures.—These difficulties in the utilization of graphic methods make it necessary to continue placing considerable emphasis upon the description of the incoordinate movements actually witnessed on the surface of the ventricles. As already emphasized, the two chief difficulties in the method of direct observation are (1) the impossibility of noting simultaneously the movements that occur in diverse portions of the ventricular surface and (2) the difficulty of following the extremely rapid movements in any given area. The use of moving pictures taken at close range and at a more rapid speed than that at which they are subsequently projected obviates both of these difficulties and in addition allows considerable magnification of the quiverings occurring in individual areas of the ventricle. Such films or isolated portions of them can be repeatedly thrown upon a screen and reviewed again and again. The observer focuses his attention first upon one and then upon another area or feature of the film itself. By doing this repeatedly in many experiments the authors feel that their conception of the character of the fibrillary process has been greatly extended.

THE NATURAL COURSE OF VENTRICULAR FIBRILLATION

Fibrillation in the anesthetized dog continues from fifteen to fifty minutes (average twenty-four minutes) before complete standstill takes place. The characteristics of the fibrillating ventricles were studied in 18 dogs by taking moving pictures and electrocardiograms during the natural course of such fibrillation.

The method of experimentation was briefly as follows: Dogs were anesthetized with small doses of morphine and sufficient quantities of sodium barbital administered intravenously. The chest was opened, the heart exposed, the pericardium severed and stitched to the lateral walls of the chest so as to form a cradle for the heart. Moving pictures were taken by means of a Bell-Howell camera on 16 mm. film at a rate of 32 exposures per second. The camera supplied with a Zeiss 25 mm. F-2.7 lens was mounted at a distance of 12 to 18 inches from the anterior surface of the heart. Adequate illumination was furnished by three 1000 watt lamps, so that pictures could be taken with the diaphragm stop between 2.7 and 4. Orthochromatic film was used in the first experiments, but great improvement resulted from the subsequent use of panchromatic film. In many experiments, special methods were adopted for locating specific areas upon the ventricular sur-

face. In some cases, small beads were fastened with horsehair by a delicate stitch through the epicardium. In others, white stitches with large knots were similarly placed. In still other experiments, the expedient of thrusting small white-headed pins into the heart itself was tried, and finally the epicardium was bespeckled with small dots of white Duco paint. Finally, good use was made of the reflections of the lamp filaments from the glistening surface of the epicardium. These produced mirror phenomena which frequently brought out the peculiar characteristics of the fibrillating movements to the best advantage.

Coincident with the moving pictures, electrocardiographic records were taken by standard leads. The moments when such records were being inscribed were signalled by a marker operating at the side of the heart. In this way comparisons between the electrocardiographic deflections (usually taken by Lead II) with the actual movements shown in cinematographic records could be made at any time.*

TRANSITIONAL CHANGES IN THE CHARACTER OF FIBRILLARY CONTRACTIONS

From the onset of fibrillation until the ventricles naturally become quiescent, many variations occur in the appearance of the ventricles and in the electrocardiograms. While these changes are transitional in nature, there is sufficient abruptness in the changes to make it permissible for descriptive purposes to divide the course of fibrillation into stages:

(a) The Initial Tachysystolic Phenomena.—Fibrillation of the ventricles usually begins with a very few (2 to 8) peristaltic waves which sweep rapidly over the ventricular surfaces in the general direction of the superficial muscle bundles. Frequently they seem to arise from a single focus located either in the central region or pulmonary conus of the right ventricle and in this case are fairly regular in period and direction. This has been ascertained by counting the number of photographic exposures between the completion of the separate waves. In other cases, however, the waves appear to spread in several directions, beginning sometimes on one area and at other times on several surface regions. The larger contraction waves sweep over both ventricles; e.g., a contraction may originate in the central region of the right ventricle, move in both directions, reaching the base of the right ventricle and the apex of the heart approximately simultaneously; or the wave may start at the pulmonary conus of the right ventricle, sweep over the anterior surface of the right ventricle, apparently hurdle the coronary vessels and pass on uninterruptedly to the left ventricular apex. These first movements are accompanied by character-

*Cinematographic films demonstrating the changes to be described have been exhibited before the American Physiological Society (1928), Cleveland Academy of Medicine (1928), Pacific Northwest Medical Assn. (1928), Buffalo University Medical School Alumni Association (1929), and International Congress of Physiology (1929).

istic deflections in the electrocardiograms which are illustrated in Figs. 1, 2*B*, and 3*A*, between the points labelled 1 and 2. They are of large size, rise and fall rapidly, and occupy an interval of 0.08 sec. or more. Beat by beat their amplitude decreases, their gradients become more gradual, and the periods of the entire beat decrease, i.e., the calculated ventricular rate becomes progressively faster. When the periods are reduced to 0.1 or 0.08 sec., i.e., corresponding if continued to a ventricular rate of 600 to 750 per minute, the process abruptly passes into the next phase.

As shown in Fig. 1, each electrical deflection is accompanied by a small but distinct elevation of intraventricular pressure, though the aortic pressure declines steadily because no blood is expelled. All the evidence, therefore, favors the view that these beats are still coordinated in the sense that they sweep over the ventricles in regular paths and develop sufficient force to elevate intraventricular pressure.

In the dog's heart this tachysystolic stage usually lasts less than 1 second; in fact, it usually sets in before faradic stimulation has ceased. This is not surprising in view of the high contraction frequencies reached.

(*b*) *Stage of Convulsive Incoordination.*—The initial stage already described leads into a second in which waves of contraction with distinctly different rhythms and sequence pass over the ventricles. This stage ordinarily continues from fifteen to forty seconds, but in several instances it was shorter.

When any small circular area 2 to 3 cm. in diameter is carefully observed in projected moving pictures, it can easily be seen that the frequency has increased and that the sequence of contractions is less regular. The localized contractions appear to be rather forceful, but successive contraction waves do not spread over identical paths or involve the same surface groups of muscle tissue. By comparing several such areas, it is noted that the frequencies differ and bear no relation one to the other. Owing to the extreme incoordination, no pressure oscillations occur within the ventricles.

This stage of incoordination is characterized by large, rather violent oscillations of the galvanometer string. They are illustrated in Figs. 1 and 3*B*, between points 2 and 3. In these instances the successive waves vary considerably in contour, amplitude and period, but the frequency, calculated over a considerable portion of the curve, may be placed between 600-660 per minute. Occasionally the electrocardiographic oscillations become even more rapid while this form of incoördination is in progress. This is well shown in Fig. 2*B* between the points 3 and 4 where they attain the alarming frequency of 1,560 per minute. Careful comparisons of electrocardiograms and cinematographic records during such intervals have clearly demonstrated, however, that these rapid electrocardiographic deflections do not portray

the contraction phenomena visible on the surface of the heart, for the latter are always much slower during this stage of fibrillation. In the instance shown in Fig. 2 the stage terminated at point 5.

When the ventricles are held in the palm of the hand, a fluttering, undulatory, convulsive sensation is experienced, no doubt due to the

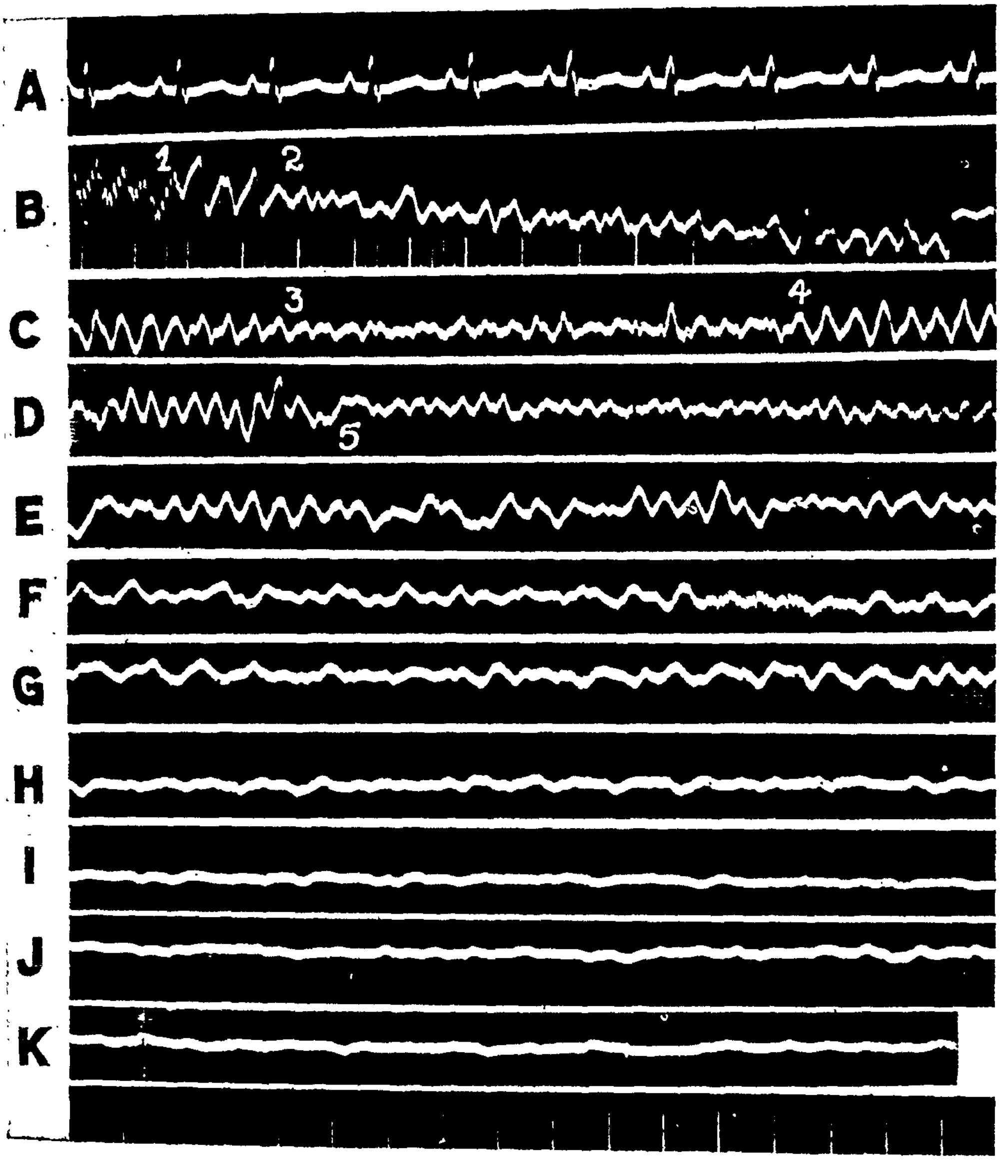

Fig. 2.—Segments of electrocardiogram (Lead II) taken at various stages during the course of fibrillation (043). *A*, control; *B*, and *C*, immediate effects; *D*, after thirty seconds; *E*, after one min.; *F*, after one and one-half min.; *G*, after two min.; *H*, after five and one-half min.; *I*, after sixteen min.; *J*, after twenty min.; *K*, after twenty-one min. Time 0.04 and 0.2 sec.

fact that blocks of myocardium are contracting with different strengths and at different rates and rhythms. From the convulsive appearance of the heart and the fact that no periodic changes of intraventricular pressure are produced, we have designated it as the stage of convulsive incoordination. The terms *coarse fibrillation, flutter, un-*

dulation, ondulation, Wühlen und Wogen, etc., used by others might be applied but are avoided since we are not certain that they were always limited to the particular stage we desire to describe.

(*c*) *Stage of Tremulous Incoordination.*—This type of incoordination ordinarily follows upon the coarse, convulsive type and continues for two or three minutes. The entire surface of the ventricles presents the appearance of multitudes of shivering and shimmering motions of a very rapid sort. The contraction waves spread very rapidly and apparently only short distances. We have seen many instances where reflected light beams from the epicardium give the impression of darting wriggling worms or of contraction waves chasing each other in circles. When the heart is palpated, it gives the impression that has been so aptly described as similar to that obtained when the hand is thrust into a can of worms. This stage is undoubtedly comparable to the types of fibrillation described as *delirium cordis, mouvement fibrillaire, Herz-zittern, fibrillary twitchings,* etc., by others, but for reasons already given we have purposely avoided previously used terms.

Viewed as slow motion picture films, the process is seen to consist of localized contraction waves spreading over short distances or circling around in very limited areas. Their speed of propagation is not actually increased. The frequencies of these visible contractions in different regions of the ventricular surface are apparently unrelated. We have studied one instance carefully in which the rate varied between 600 and 1800 per minute in different portions of the right ventricle. We have tried numerous and laborious expedients for interrelating these rapid contraction circles in selected regions, but after diligent attempts we have found this impossible.

During this stage the electrocardiographic deflections increase in frequency and diminish in amplitude. They are shown in Fig. 2*D* after point 5 where their frequency is about 1140 per minute and in Fig. 3*C* where they average about 1520 per minute. Counts in other experiments give ranges from 1100 to 1700 per minute. Pressure curves recorded from the ventricular cavities show that these rapidly executed incoordinate contractions of extremely small muscle units not only maintain the previous existing intraventricular tension but sometimes actually increase it somewhat. The pressure curves, however, continue as a straight line and show no evidence of oscillations except occasionally those due to continuing auricular contractions.

(*d*) *Stage of Progressive Atonic Incoordination.*—The stage of rapid incoordinate contractions just described is gradually replaced by a stage of coarse atonic incoordination, so designated because the visible waves not only become coarser and slower, but they no longer maintain the previous small even elevation of intraventricular pressure. We are not aware of any previous description of this stage; most observers limiting themselves to the phenomena characterizing the earlier stages.

The ventricular surfaces show characteristic changes in appearance. During the early portion of this coarse atonic stage of fibrillation, wavelets of contraction are seen to spread over small areas of the ventricle. The rhythm is obviously different in different regions. The rate of propagation slows down materially, the frequency of movement is reduced, and the contractions are obviously less vigorous. At first such movements occur over the entire ventricular surface, but gradually they decrease in intensity until certain areas display none. The quiescent areas increase in number until finally only the slightest movements remain in a few regions. The areas which usually pulsate longest in this manner are those which lie near the coronary vessels, usually to the right side of the septal demarcation. The last movements to be seen are mere quivers, perceptible only when beams of light from a lamp are reflected from the moist and glistening epicardium. Frequently, when all visible movement has apparently ceased and no sensation can be felt by the finger or heard on auscultation, the electrocardiograph still continues to show minute irregular oscillations. Whether these are accompanied by contractions in the deeper layers of the ventricle or whether conduction occurs without mechanical shortening under such circumstances, cannot be decided with finality.

The nature of the electrocardiographic oscillations up to the final cessation of all movement is shown in Fig. 2, segments *E* to *K*. At first, the oscillations are fairly large; indeed they resemble those occurring during the early stage of convulsive incoordination. Their frequency ranges from 540 to 720 in Fig. 2. The amplitude of the deflections gradually decreases until toward the end only small oscillations remain. The frequency then also diminishes, e.g., in Fig. 2*K* the frequency is about 360. These changes in rate correspond reasonably well with movements visible in cinematographic records, but obviously the amplitudes of the deflections in the early part of this phase bear no relation to the intensity of fibrillary contractions.

Auricular Contractions During the Course of Ventricular Fibrillation.—The auricles maintain a regular rhythm for a variable length of time. Sometimes their contractions terminate before ventricular fibrillation ceases and at other times they outlast the fibrillation. The changes in the auricles are those common to other forms of asphyxia. The auricular rate soon decreases, the contractions first increase but soon decrease in vigor. It should be borne in mind that the electrical records of ventricular activities may be periodically modified by electrical variations due to auricular contraction. Very early the rate of propagation is reduced. Peristaltic waves sweep over the auricle at slow rates, giving a beautiful visible demonstration of the successive contractions of adjoining fractions. Frequently heart-block develops between the right and left auricles. On several occasions independent rhythms have been observed, suggesting that a rhythmic center becomes active in the left auricle.

THE CHANGES DURING POTASSIUM INHIBITION

The earlier manifestations of fibrillation transpire so quickly that potassium salts cannot be administered easily until the stage of tremulous incoordination has supervened. Cinematographic and electrocardiographic records from eight experiments were carefully studied. They consistently showed that potassium salts do not modify the stages of the fibrillary process; they merely hasten the process. The fifteen to fifty minutes naturally required for fibrillation to run its

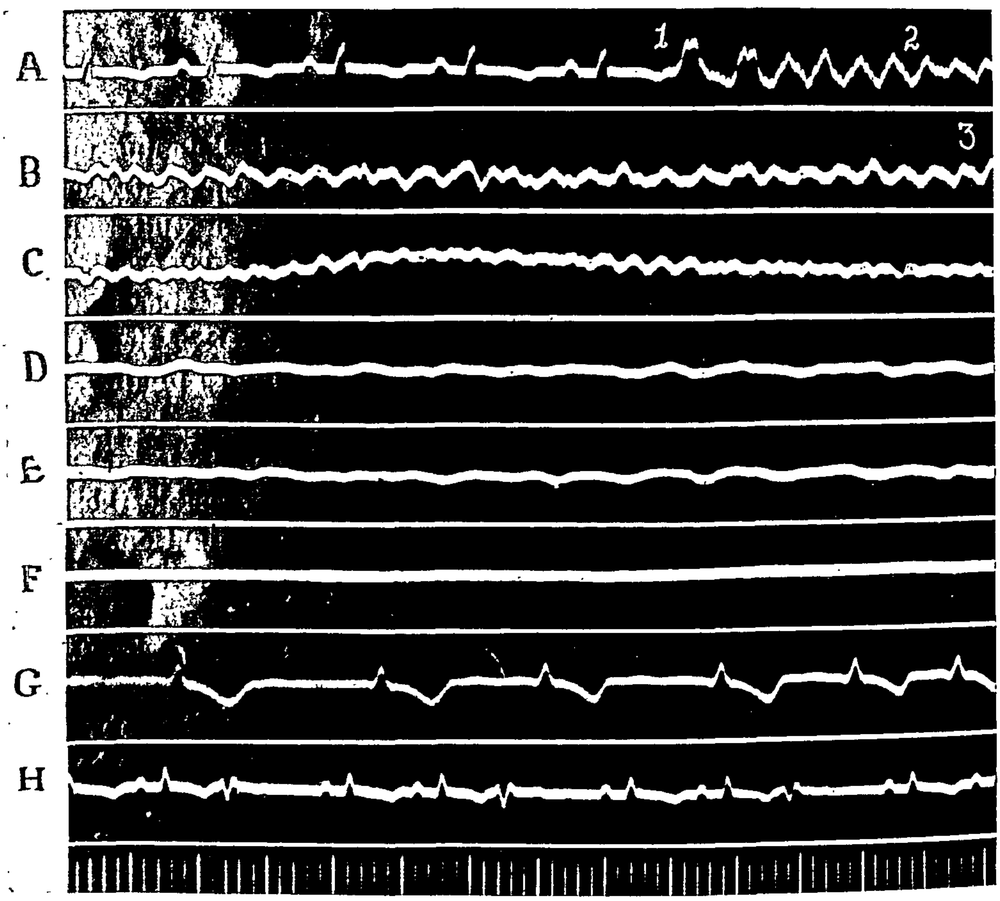

Fig. 3.—Segments of electrocardiogram (Lead II), showing the early stages of natural fibrillation, the effects of KCl and of revival following use of $CaCl_2$ (O-42). *A*, control and initial tachysystolic stage; *B*, coarse incoordination, one and one-half min. later; *C*, tremulous incoordination after two min.; *D*, one min., after use of KCl; *E*, two min. after; *F*, two and one-half min. after; *G*, initial indioventricular beats, recorded nineteen minutes after fibrillation first started; *H*, thirty min. after record *H*. Time 0.04 and 2 seconds.

course are often shortened to one or two minutes. Projected moving pictures show that the fine fibrillary waves in any region recur less frequently and spread more slowly without involving larger areas. On the contrary, the active regions gradually diminish, leaving motionless areas over the entire surface of the heart. The vigor of the localized contractions also diminishes visibly, until large areas are entirely quiescent. Feeble, slow contractions finally remain only in very re-

stricted areas, the anterior region of the right ventricle near the interventricular sulcus being the usual area in which feeble contractions persist longest.

The electrocardiographic curves also reveal no new features, but the entire process normally present runs its course more rapidly. That portion of the atonic stage which is characterized by large deflections is particularly affected. It is either very short or does not appear at all. Fig. 3 is an example of the characteristic electrocardiographic changes. Segments *A*, *B* and *C* illustrate the course of events during the first two minutes of natural fibrillation. The record shown as segment D was taken one minute later, i.e., fifteen seconds after injection of KCl. The records reproduced as segments *E* and *F* were taken at additional intervals of twenty and twenty-five seconds respectively. Almost immediately the amplitude of oscillations greatly diminished and their frequency was reduced to 240 per second in segment *E*. Fibrillation was completely abolished (segment *F*) one minute after completion of the injections.

It should be added that visible auricular contractions which normally persist for many minutes also promptly stopped. The auricles quickly came to a complete standstill. This demonstrates that potassium diffuses quickly through fluids in the cavities of the heart.

THE COURSE OF REVIVAL AFTER USE OF CALCIUM AND MASSAGE

After intraventricular injection of calcium salts and after the ventricles have been massaged for several minutes in such a way that each compression causes a slight elevation of aortic pressure, it is noticed that the ventricles respond to mechanical stimuli or compression. Similar responses may be obtained by gentle taps or single electric shocks. The ventricles recover their functions of conduction and contraction prior to regaining their ability to generate spontaneous impulses. The auricles are not yet contracting automatically; the nodal structures likewise have not regained their automaticity. Within a comparatively short time—a matter of ten seconds in some experiments and one to two minutes in others—spontaneous ventricular beats begin. Projected moving pictures show clearly the broad waves of contraction spreading over the ventricles. Beginning over the central region of the right ventricle they usually sweep upward toward the base of the right ventricle, although downward moving waves of contraction were witnessed in two instances. In the case of the left ventricle, they start at the apex, move upward along the coronary vessels, then to the left and toward the base. One instance was found in which the contraction waves had the ratio of 3:52, but, as a rule, they have the same tempo. The waves appearing over the surface of the two ventricles are not quite synchronous, however, sometimes the right and sometimes the left ventricular waves are in the lead.

As these slightly asynchronous waves gradually become stronger, the ventricles undergo a curious deformation, each beat being not unlike that seen when rapid ventricular tachycardia is produced by stimulating one ventricle artificially. Since each of these contractions elevates mean arterial pressure, it must be accompanied by elevations of intraventricular pressure. Unfortunately, we have not succeeded in recording reliable intraventricular pressure curves of this event.

At the same time that the idioventricular rhythm develops or slightly thereafter, the auricular beats return. Frequently the left auricle beats alone; again both auricles beat at different rhythms; and

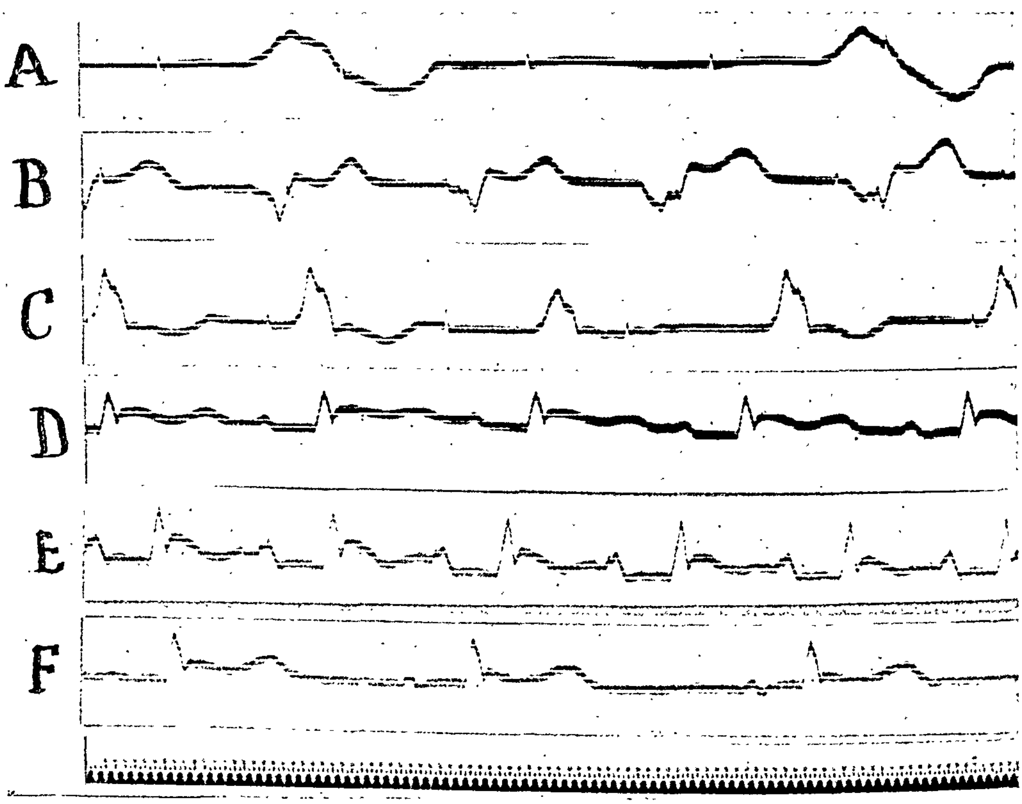

Fig. 4.—Electrocardiograms (Lead II) showing mechanisms in recovery from fibrillation. Description in text. Time 0.02 sec. (O-70, VI-XI).

finally a coordinated rhythm is established. Impulses do not yet reach the ventricles, which continue to beat with an idioventricular rhythm. This is also demonstrated by electrocardiographic tracings. Segment *G* of Fig. 3 shows a series of such idioventricular beats of increasing frequency which were recorded after an initial period of less regular action. They indicate that a single ventricular focus dominates the rhythm. This is not always the case, however, as is shown in the tracings of Figs. 4 and 5. Comparison of segments *A, B,* and *C* of Fig. 4 show clearly that the pacemaker shifted. This is partly due to the fact that a more rhythmic center functionates but not necessarily so. Thus the rate was 58 per minute in segment *C* and 120 in segment

B. Dynamically, beats originating in different centers were equally effective, for the blood pressure altered with the heart rate. Frequently, also, successive stimuli arise from different foci; a struggle for supremacy in the idioventricular rhythm apparently takes place. This is illustrated in segments *A*, *B* and *C* of Fig. 5, which show records obtained on recovery from a second fibrillation which had been induced approximately one hour later in the same animal.

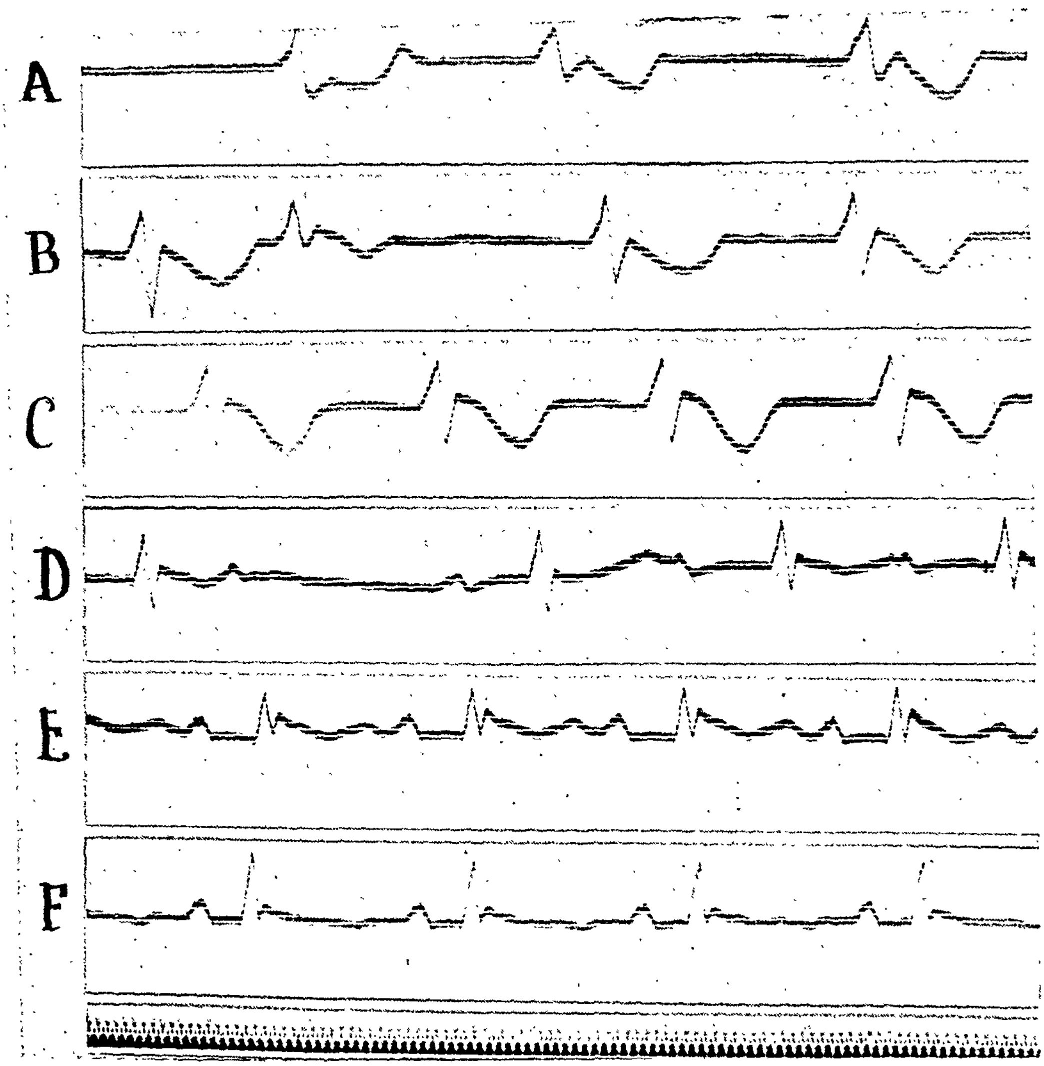

Fig. 5.—Electrocardiograms (Lead II), showing mechanisms of recovery *from* a second fibrillation in the same dog. Time 0.02 sec. Description in text (O-70, XV-XX.)

The development of this idioventricular rhythm is of greatest importance in tiding the animal over the last few critical minutes still remaining before irreparable damage is done to the central nervous system. It often precedes the redevelopment of a sinus rhythm for the auricles and, at all events, establishes effective beats capable of maintaining a reasonable blood pressure level during the interval that complete A-V block persists.

The fact that revival is inaugurated by an idioventricular rhythm is additional positive evidence that our recoveries were not spontaneous or due to chance. Spontaneous recovery, such as occurs frequently in the cat's heart and occasionally as a special phenomenon in sensitized dogs' hearts, is different in nature. Fibrillation ceases promptly, a long post-undulatory pause follows, and then a regular supraventricular beat reappears immediately.

After revival by calcium, associated with massage, such a rhythm only develops subsequent to an idioventricular rhythm of several minutes' duration. The change in pacemaker is quite abrupt. Previous to its development an auricular beat dominated by the sinus node makes its appearance, auricles and ventricles beating with independent rhythms. Quite suddenly the total block is lifted, and the ventricles begin to beat in sequence with the auricles. The electrocardiographic changes typical of this condition are shown in the lower records of Figs. 4 and 5. The normal P, R and T sequence obtains. The records taken immediately after development of a supraventricular rhythm differ from the normal in several ways. Usually, as in the record of Fig. 5*D*, the P-R interval is prolonged, but this is always reduced to normal values within five or six minutes or less (cf. Fig. 4*F* and Fig. 5*F*). The deflection is often abnormal in contour, reminding one of the variable changes that follow coronary ligation. Frequently the descending level of R does not return to the base line but grades into it by a broad declining plateau or is followed by a rounded hump. These features are often more pronounced than in the case of segments reproduced as Figs. 4*E* and 5*E*. After these abnormalities disappear, the T-wave may become accentuated as in Fig. 4*F*, but frequently it is negative, as shown in Figs. 3*H* and 5*F*. The normal rhythm once regained becomes permanent. A relapse to an idioventricular type was not observed. Not infrequently it is interrupted by premature systoles of auricular, nodal or ventricular origin, as in Fig. 3*H*. Gradually the normal characteristics of the electrocardiogram reappear. The P-R interval is reduced to normal values, and the ventricular waves regain their natural appearance. That the heart has not been injured permanently, either by the concentrated salt solutions employed or by the period of temporary anemia, is thus conclusively established.

SUMMARY

1. The natural course of events from the onset of fibrillation following faradic excitation to complete diastolic rest was studied by recording electrocardiograms and moving pictures simultaneously. In addition, intraventricular pressure curves were optically recorded during a number of experiments. The changes taking place when fibrillation was inhibited by intraventricular injections of 5 per cent KCl and the process of recovery following similar injections of 5 per cent $CaCl_2$

solutions combined with massage, were investigated by the same means.

2. Fibrillation induced by faradic stimulation continues naturally for fifteen to fifty minutes and may be divided into 4 stages, on the basis of surface changes, electrocardiographic deflections and intraventricular pressure variations.

3. The initial stage of tachysystole lasts less than one second and is characterized by the spread of rapidly recurring but coordinated contraction waves, by large electrocardiographic deflections with steep gradients and by definite if small intraventricular pressure variations.

4. The second stage of convulsive incoordination ordinarily lasts fifteen to forty seconds and is characterized by rapid irregular localized contractions which spread short and variable distances over the heart. They are accompanied by large electrical deflections, 600 or more per minute, which vary considerably in size, amplitude and contour.

5. The third stage of tremulous incoordination ordinarily continues two or three minutes and is characterized by multitudes of irregular yet forceful shivering or trembling motions, each spreading very short distances and with highly variable frequencies over different surface regions. They give rise to small irregular electrocardiographic oscillations having frequencies between 1100 and 1700 per minute, and are capable of increasing the intraventricular pressure level slightly.

6. The fourth stage of atonic incoordination is characterized by feeble wavelets of contraction spreading irregularly and at slow rates over small areas until more and more areas become quiescent, and finally the very slightest movements remain in a few areas only. The electrical deflections perhaps become slightly more regular in contour and spacing, but their amplitude becomes progressively smaller, and their frequency is gradually reduced to 400 per minute or less.

7. Potassium chloride injected into both ventricular cavities does not modify the stages through which fibrillation naturally passes; it merely hastens the process so that fibrillation stops within an average period of 2.4 minutes.

8. Intraventricular injections of $CaCl_2$ after potassium inhibition combined with massage, first inaugurate a coordinated idioventricular rhythm, characterized by slow waves of contraction sweeping over the two ventricles asynchronously but in coordinated fashion. After a short interval, a supraventricular rhythm is reestablished, the electrocardiogram regaining all its normal characteristics.

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ELECTROCARDIOGRAPHIC STUDIES BEFORE AND AFTER CHEST OPERATIONS*†

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In extensive operations on the chest possible damage to the heart is of ever present concern to the surgeon. In chest surgery there are the peculiar local factors of displacement, sudden changes in pressure, changes in the pulmonary circulation in addition to the general factors of anesthesia, surgical shock and infection. The ultimate damage to the heart, if any, by these local factors can be determined only by careful clinical observation of the patient during the years following operation.

Some time ago it occurred to us that the immediate displacement of the heart frequently observed following chest operations might have a part in determining either the convalescence or subsequent state of health of the patient. As a possible aid to estimating the effect of displacement on cardiac function, electrocardiographic studies were made on a selected group of twenty-two of the patients admitted to the services of one of us (R. B. B.). Each patient was referred for electrocardiograms before and immediately after operation. Those patients who required multiple stage operations were referred after each operation. X-ray plates of the chest were made before and after each operation.

The results were studied from the following points of view:

1. X-ray evidence of cardiac displacement.
2. Changes in the electrocardiogram which would indicate structural or functional change in the heart.
3. Changes in the electrical axis (which can be interpreted as indicating change in the anatomical axis).

The patients have been grouped according to the type of operation. Some had more than one type of operation. Some had multiple stages of the same operation.

Extrapleural Thoracoplasty.—(Seven cases.) The operation of extrapleural thoracoplasty is performed on patients with unilateral, or virtually unilateral, pulmonary tuberculosis who have not responded to sanatorium treatment. The object is to collapse and immobilize the affected lung. This is accomplished by removing segments of the ribs posteriorly from the 1st to the 11th inclusive. The operation is performed in two or more stages.

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In this series four patients had right-sided lesions. In all of these the heart after operation was displaced to the left, according to the postoperative x-ray findings. The extent of displacement varied from slight to moderate. All showed some functional change as evidenced by decrease in amplitude of the R-wave or inversion of the T-wave or both.

One patient, a young woman, developed inversion of the T-wave in Lead II and an increase in the inversion of T-wave in Lead III following the first stage. Following the second stage the inversion was much more marked and was of the coronary type. There was evidence of considerable change in the anatomical axis of the heart, and there were also clinical signs of severe cardiac embarrassment, following the second stage. Displacement of the heart, according to x-ray evidence, was only moderate. Respiratory mobility of the heart was increased slightly after the second stage operation in two cases and remained unchanged in two. The electrical axis changed 32° in the direction of right axis deviation in one patient, and 45° in the direction of left axis deviation in another. In the other two there was no change, or so slight a change as to be within the limits of error.

According to Lewis[1] change in the electrical axis is a rough measure of change in the anatomical axis of the heart. In order to determine accurately any actual change in electrical axis after operation the range of variation in the axis during respiration was measured in each curve before and after operation, and the axis obtained in similar phases of the two curves compared. We may reasonably infer that in two patients there was an appreciable change in the anatomical axis of the heart. The one showing the change of 32° is the young woman referred to above.

Three patients in the group had left-sided lesions. Two showed slight displacement of the heart shadow to the right after operation. One showed slight functional change in the electrocardiogram, the other none. Neither showed structural change. Respiratory mobility was not affected. There was no change in electrical axis in one; in one a change of 10°. The third patient, a man 43 years old, was of especial interest. The electrocardiograms before operation showed evidence of structural damage (low amplitude of QRS in all leads, slight notching of R in Lead II, marked notching of S in Lead III, absence of isoelectric period in the R-T interval in all leads, inversion of T in Lead III, slight notching of P in all leads). This was the only patient showing electrocardiographic evidence of heart muscle damage prior to operation. While the changes were slight, still they were thought to be more than could normally be accounted for by his age. We have seen patients with much more marked electrocardiographic evidence of myocardial damage withstand major abdominal operations without difficulty, yet this patient died of cardiac failure on the fourth postoperative day, after an apparently well-tolerated first stage. We

TABLE I

GROUP I. EXTRAPLEURAL THORACOPLASTY

NAME	AGE	SEX	DIAGNOSIS	SITE	OPERATION	DISPLACEMENT OF HEART SHADOW, BEFORE	SHIFT OF HEART SHADOW, AFTER	RANGE OF ELEC. AXIS, BEFORE	RANGE OF ELEC. AXIS, AFTER	FUNCTIONAL CHANGE	STRUCTURAL CHANGE	RESPIRATORY MOBILITY	ANATOMICAL AXIS
RU	16	F	T. B. hydro-pneumothorax	R	Aspirated 100 c.c. air 300 c.c. fluid Thoracoplasty 11 – 6 inc.	To left	More to left	+57° to +64°	+63° to +69°	+	None	Same	Slight change
	16	F	Same	R	Aspirated 100 c.c. air 125 c.c. fluid 6 – 1 ribs	Back to previous position	Slight to left	+34° to +52°	+66° to +77°	+	None	Increased	Marked change
FI	22	F	Tbc.	L	Thoracoplasty	None	To right	None to +58°	None to +59°	None	None	No change	No change
	22	F		L	Same 2nd				None to +58°	+	Slight improvement	No change	No change
TR	24	M	Lung abscess. Bronchiectasis	R	Thoracoplasty 1st stage 6 back		To left	+35° to +42°	+39° to +43°	+	More marked	Same	No change
	24	M		R	2nd stage 6 front			+36° to +44°	+34° to +48°	+		Increased	Slight total change
FI	26	F	Tbc. pyo-pneumothorax	R	Drainage Emp. 11 – 1 ribs	Slight to left	Slightly more to left	+58° to +79°	+69° to +90°	Slight	None	Same	Slight change
RU	21	M		L	7 – 4 ribs		Slight to right	+42° to +49°	+32° to +38°	+	None	Same	Slight change
ST	25	M	T. B. empyema	R	11 – 6 1st stage	None	No x-ray	+65° to +73°	+20° to +30°	+	None	Same	Marked change
	25	M		R	6 – 1 ribs 2nd stage		Left		+37° to +47°	None	None	Same	Moderate change
PA		M			11 – 7 1st	Died cardiac failure 4 P.O. day E. C. G. Subendocardial lesion.							

TABLE I—CONTINUED

NAME	AGE	SEX	DIAGNOSIS	SITE	OPERATION	DISPLACEMENT OF HEART SHADOW, BEFORE	SHIFT OF HEART SHADOW, AFTER	RANGE OF ELEC. AXIS, BEFORE	RANGE OF ELEC. AXIS, AFTER	FUNCTIONAL CHANGE	STRUCTURAL CHANGE	RESPIRATORY MOBILITY	ANATOMICAL AXIS
GROUP II. PHRENICOTOMY													
BR	64	M	Lung abscess	R	Phrenicectomy after pneumo.	None	To left 1 cm.	−53° to −30°	−53° to −30°	None	None	Same	No change
TR	23	M	Lung abscess. Bronchiectasis	R	Phrenicectomy after thoracoplasty	None	None	+34° to +48°	+39° to +48°	None	Improvement	Sl. less	No change
PR	24	F	T.B.C. L. lower	L	Phrenicectomy	None	Very little to right	+26° to +36°	+14° to +19°	None	None	Less	Change
WO	29	M	Bronchiectasis	R	Phrenicectomy after artif. pneu.	None	None	+79° to +83°	+77° to +87°	None	None	Marked increase	No change
GROUP III. CAUTERY LOBECTOMY													
BU		M	Lung abscess	R	Cautery lobectomy after phrenicectomy	None	None	+90° to +95°	+90° to +95°	None	None	Same	No change
GROUP IV. OPEN PNEUMOLYSIS													
WE	37	M	Lung abscess	R	Open pneumolysis c. pneumoth.	To left	More, 2 cm. to left	+94° to +103°	+100° to +144°	None	Improvement	Marked increase	Slight change
WA	21	M	T.B. art. Pneumothorax	R	Pneumolysis	To left	Much more to left	+63° to +69°	+57° to +64°	None	None	Slight increase	Slight change

TABLE I—CONTINUED

GROUP V. EMPYEMA

NAME	AGE	SEX	DIAGNOSIS	SITE	OPERATION	DISPLACEMENT OF HEART SHADOW, BEFORE	SHIFT OF HEART SHADOW, AFTER	RANGE OF ELEC. AXIS, BEFORE	RANGE OF ELEC. AXIS, AFTER	FUNCTIONAL CHANGE	STRUCTURAL CHANGE	RESPIRATORY MOBILITY	ANATOMICAL AXIS
CO	8	F	Empyema	L	Drainage	To right	2 cm. to left	+30° to +37°	+13° to +16°	None	None	Practically none	Moderate
GU	5	M	Empyema	L	Drainage	R	L	+67°	+56° to +68°	T II & III	None	Slight increase	None
AD	3	F	Empyema	R	Drainage	L	R	+69°	+73° to +82°	None	None	Slight increase	Very slight
SI	6	M	Empyema	R	Drainage	L	R	+86° to +95°	+99° to +99°	Dec. Amp. Q.R.S.	None	Slight decrease	None
HO	40	F	Pleurisy LEH.	L	Drainage	R	No change	–4° to –16°	–10° to –20°	None	None	Same	Very slight

GROUP VI. ARTIFICIAL PNEUMOTHORAX

NAME	AGE	SEX	DIAGNOSIS	SITE	OPERATION	DISPLACEMENT OF HEART SHADOW, BEFORE	SHIFT OF HEART SHADOW, AFTER	RANGE OF ELEC. AXIS, BEFORE	RANGE OF ELEC. AXIS, AFTER	FUNCTIONAL CHANGE	STRUCTURAL CHANGE	RESPIRATORY MOBILITY	ANATOMICAL AXIS
RA	30	M	Tbc. R	R	1500 c.c. Pneumo.	L	More	+90° to +105°	+103° to +111°	Decreased amplitude	None	Less	Slight change
FR	26	M	Tbc. R	R	650 c.c. Pneumo.	None	None	+13° to –58°	–78° to –83°	None	None	Less	Marked change
BR	64	M	R. middle lobe abscess	R	650 c.c. Pneumo.	None	None	–26° to –50°	–45° to –59°	None	None	Less	Moderate change

do not wish to draw unwarranted conclusions from a single experience, but since this was the only fatality and was a cardiac one, it does suggest that patients showing electrocardiographic evidence of structural change in the heart may be poorer subjects for chest surgery than for other types of operative procedure.

Phrenicectomy.—The aim of this operatoion is to paralyze the diaphragm for the purpose of partially immobilizing and compressing the lower lobes of the lung for such conditions as lung abscess, bronchiectasis, or tuberculosis. The phrenic nerve is exposed in the posterior triangle of the neck where it crosses the scalenus anticus muscle. The nerve is cut and a portion of the distal section is evulsed. The diaphragm on that side becomes paralyzed, assumes a position from one to two and a half inches higher than the other side and remains practically immobile during respiration.

In this group we included four patients. In three the operation was performed on the right side. One showed shifting of the heart shadow, two did not. In one the respiratory mobility of the heart was slightly less, in one slightly more after operation, 5° and 6° respectively. One showed some structural or functional improvement as indicated by the disappearance of notching of R in all leads. This patient previously had a two stage thoracoplasty and is included in that group. It was following the thoracoplasty that the notching of R developed. The disappearance of this abnormality can hardly be attributed to the phrenicotomy. It is more likely due to the time which elapsed between the two operations and the natural recovery processes incident thereto. There was no change in the anatomical axis as indicated by the electrical axis.

The one patient having the left-sided lesion showed a slight shifting of the heart shadow to the right. There was no structural or functional change as indicated by the electrocardiogram. There was slightly lessened respiratory mobility (5°). The electrical axis changed 12° toward left axis deviation, suggesting slight change in the anatomical axis. These last changes may be the result of immobilization of the diaphragm by the operation.

Cautery Lobectomy.—This operation consists in fixing the lung to the chest wall by artificial adhesions if natural ones do not already exist, and thereafter cutting a window in the chest, removing a lobe or a portion of a lobe of lung piecemeal by means of a cautery. The operation in this case was performed for multiple abscesses and bronchiectasis. The fact that the lungs, and therefore the mediastinum, are firmly fixed by adhesions means that the heart is not displaced by the operative procedure. However, we investigated this one case of cautery lobectomy, in which a large amount of pulmonary tissue had been re-

moved to see whether or not a possible change in the size of the pulmonary circulation would give rise to any changes in the electrocardiogram.

The patient showed no change in any of the factors under consideration.*

Open Pneumolysis.—By pneumolysis is meant the cutting of such adhesions as may fix the lung to the chest wall. Both of the two cases included in this investigation had a large cavity in the right lung—one a tuberculous cavity of the right apex, the other a nontuberculous abscess in the middle lobe. In both of these cases bands of adhesions prevented the accomplishment of a collapse of the lung by artificial pneumothorax. The operation consisted of opening the chest cavity, tying the large veins which were found in the adhesions, cutting the adhesions, and then closing the chest tightly. Immediately after the chest wound was closed, artificial pneumothorax was induced and in both instances complete collapse of the right lung was obtained.

In both cases the heart shadow was displaced to the left before operation and considerably more to the left afterward. In one the left border touched the rib shadow after operation. There was no functional or structural change in either. Respiratory mobility was increased in both; in one 33°, in the other 4°. Change in the electrical axis was only 6° each but in opposite directions in the two cases. This suggests very little if any change in the anatomical axis in spite of the marked shift to the left of the heart. Also the inconstancy of the direction of the electrical axis change is of interest.

Empyema With Drainage.—In this group five patients were included. These five patients were treated by the so-called closed method of drainage. Pneumothorax was never present throughout the entire course of treatment. Thus any deviation of the position of the heart from normal before operation was never for an instant increased but steadily diminished from the time drainage was started until the patient was cured. Two patients had right-sided lesions. In both of these the heart shadow was displaced to the left before operation and shifted back to the right afterward. Respiratory mobility was affected in both, showing a decrease of 9° in one and an increase of 9° in the other. One patient showed slight functional change as indicated by decrease in amplitude of QRS in all leads. Neither showed any change in the anatomical axis.

Three patients had left-sided lesions. All showed displacement of the heart shadow to the right before operation and shift of the shadow back to the left afterward. One showed slight increase in respiratory

*Incidentally a few years ago one of us had occasion to remove the entire lower lobe of the left lung, thus leaving the posterior pericardium exposed except for a layer of pleura and granulation tissue. In this case electrocardiograms of the heart were taken by applying the electrodes directly to the pericardium, but no noteworthy findings resulted.

mobility, the other two no change. In one there was slight functional change. T_3 which was inverted became upright, and T_2 increased in amplitude. There was no evidence of structural change. One showed some change in anatomical axis as indicated by a change of 17° in the electrical axis toward left axis deviation.

Artificial Pneumothorax.—The aim of an artificial pneumothorax is to collapse and immobilize one lung. The procedure is applicable in certain cases of unilateral or virtually unilateral pulmonary tuberculosis, bronchiectasis, or lung abscess. The collapse of the lung is obtained by inserting a needle into the pleural space and allowing varying amounts of air to enter.

This group includes three patients, all with right-sided lesions. The heart shadow did not shift in two and shifted slightly to the left in one. There was decreased respiratory mobility in all, varying from 8° to 66°. There was no functional or structural change. In one the electrical axis changed 13° to a frank right axis deviation, in one it changed to a frank left axis deviation, in the other with a left axis deviation to begin with it changed 19° more in the left axis direction. A change in the anatomical axis in all is thereby suggested. The last results are interesting in view of the recent evidence that axis deviation does not necessarily mean preponderant hypertrophy of one or the other ventricle, since the curves showing axis deviation were taken within twenty-four hours after operation and before hypertrophy had chance to take place. They are in accord with what Cohn[2] and others have shown, namely, that the electrical axis is dependent in part on the anatomical axis and the position of the heart in the chest with reference to the lead-off electrodes.

SUMMARY

Of a total of twenty-four observations the relation of shift in the heart shadow to change in the anatomical axis, as indicated by change in the electrical axis, is as follows:

1. Shift with change 11.
2. Shift without change 5.
3. Change without shift 3.
4. No shift and no change 5.

Thus in 66.6 per cent the evidence of change in the anatomical axis coincided with the x-ray findings. The degree, however, was not proportionate. The two cases showing the most marked shift in the heart shadow showed only slight changes in the electrical axis (6° and 4°) practically within the limits of error. One case showing a change of 32° in the electrical axis showed only slight shifting of the heart shadow. Also two cases showing a change of 45° and 91° had no shift of the heart shadow. These results may be interpreted to indicate that the

heart may be considerably displaced as a whole to one side or the other in the chest without changing its anatomical axis, or it may rotate considerably on its anatomical axis without changing its relative position in the chest.

CONCLUSIONS

1. X-ray evidence per se of displacement of the heart is of relatively little importance in determining cardiac embarrassment as compared to electrocardiographic evidence of functional or structural change.
2. Change in the anatomical axis is independent of the direction or extent of displacement as shown by x-ray films and probably depends upon other factors, such as mediastinal adhesions, etc.
3. So far as this series goes, in thoracoplasty there is more cardiac disturbance, from the point of view of the electrocardiogram in operations on the right side than in those upon left.
4. Conduction time was not influenced by the operative procedures in any of the patients of this series.
5. Respiratory mobility may be either increased, decreased, or unaffected, regardless of the side of the lesion and operation. It is most constantly affected by artificial pneumothorax and was markedly decreased in all three patients of this series.
6. Of the operations of this series, that of thoracoplasty seems to put the greatest strain on the heart. This may go hand in hand with the clinical evidence which has indicated the need for multiple stages.

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Department of Clinical Reports

RAPID VENTRICULAR RHYTHM PRODUCED BY PRESSURE OVER THE PRECORDIUM REPORT OF A CASE*

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THE case reported in this paper is that of a rapid ventricular rhythm with A-V conduction normal but with V-A conduction blocked (retrograde block) and a ventricular rate higher than the auricular rate.

CASE REPORT

The patient is a schoolgirl, 13 years old, who had three severe attacks of rheumatic fever with polyarthritis at the ages of 5, 8 and 11 years. She had rheumatic nodules at 11, and a moderate attack of tonsillitis at 10. Heart disease was discovered at the age of 5 during the first attack of rheumatic fever. She had no symptoms until the age of 10 when she began to complain of some dyspnea, palpitation and precordial pain. At present she attends school and is able to meet the ordinary demands of school life. She has never been confined to bed with congestive heart failure.

On October 6, 1927, she was referred to the Adult Cardiac Clinic at Bellevue Hospital. An examination of her heart showed that it was much enlarged, extending to the anterior axillary line. There was considerable precordial heave and tenderness. The first sound at the apex was snappy, the second sound was reduplicated. At the apex there was a localized rumbling diastolic murmur and a harsh blowing systolic murmur, which was transmitted to the left and around the back as far as the right axilla. Roentgen-ray examination showed cardiac enlargement characteristic of mitral disease. The routine electrocardiogram was negative except for sinus arrhythmia. The diagnosis upon admission was rheumatic heart disease (inactive), enlarged heart, mitral stenosis and insufficiency, sinus arrhythmia, class 2A (slight limitation of cardiac functional capacity).

She was seen at the clinic every two weeks and frequently in the ward where special studies were made. Oral temperatures were taken at each visit, and in all instances except four the temperature range was between 99° and 100°, the average being 99.6° F. These temperature readings were checked at different periods during the day and were invariably above normal. As no cause could be found for this consistent elevation of temperature, it was thought that an active rheumatic infection of the heart was probably present. This was also borne out by the fact that precordial tenderness was consistently present. This sign of rheumatic activity has been pointed out by Swift and Hitchcock.[1] Frequent blood counts were taken and found normal except for a relative lymphocytosis. The urine and Wassermann examinations were normal.

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At one of the early routine examinations at the clinic, it was observed that the heart developed a rapid rhythm when pressure was applied upon the chest wall and that when the pressure was released the heart returned to normal. The arrhythmia was elicited at will by thumb pressure and could be maintained without interruption for at least one minute. Through the entire period of observation, from October, 1927, to May, 1929, the method never failed, although recently it has been difficult to elicit the arrhythmia or to maintain it for long stretches. The rapid rate was not attended by any cardiac symptoms except palpitation and some precordial distress, especially when the tachycardia was maintained beyond 10 or 15 seconds. Electrocardiographic tracings identified the rhythm as of ventricular origin.

Just after the application of pressure to the precordium a change of rhythm occurs which persists only while the pressure is applied and immediately returns to normal on the release of pressure. (Fig. 1.) The ventricular rate is faster and the QRS complexes are of lower voltage (this is true also of Leads I and II). The ventricluar rate increases from the normal cycle lengths of 0.56 sec. to varying cycle lengths of 0.44 to 0.36 sec. during the application of pressure. There is no widening of the QRS, and for this reason it is probable that the origin of the ectopic rhythm is above the bifurcation of the bundle. The auricular rate and rhythm remain entirely unchanged, so that during the application of pressure the ventricles are beating at a much faster rate than the auricles. To explain this condition it must be assumed that the rapid impulses from the new ventricular pacemaker fail to reach the auricle and that retrograde block exists. However, there is evidence that conduction from auricles to ventricles is normal. This is shown by the occasional interruption in the ventricular rhythm by normal ventricular complexes, which are probably produced by impulses from the auricle (point C) because the normal P-R interval is present and the ventricular complexes are like those of the normal control. In order to interrupt the ectopic ventricular rhythm, the impulse from the auricle must arrive after the refractory period in the ventricle is over and as a necessary corollary before the ectopic impulse has been initiated. To fit in with this condition a ventricular complex which responds to an auricular impulse must be closer to the preceding ectopic beat than the next expected beat. The ventricular rhythm, however, is so irregular that one cannot anticipate the location of the next ectopic beat. The ventricular complexes resulting from auricular impulses are always very close to the preceding ectopic beat and at no time is that interval equal to 0.44 sec. which is the longest ectopic cycle length.

Only a few cases showing this type of arrhythmia have been reported. White[2] reported such a rhythm in a patient following tonsillectomy and in two others following digitalis. Hewlett[3] has reported similar tracings. In two of White's cases and in Hewlett's case the ventricular rhythm was interrupted by ventricular complexes in response to normal auricular impulses. We have been unable to find in the literature any instance in which the ectopic rhythm described above was produced by

pressure over the precordium. Condorelli[4] applied vigorous percussion in the fifth left interspace to a patient with Stokes-Adams syndrome and was able for a period of two hours to keep up a ventricular rhythm which was identical with the rate of percussion. He later induced ventricular premature contractions by direct percussion in the fifth left interspace in normal subjects. Hoffman,[5] Oppenheimer and Stewart,[6] and Fossier[7] have been able by mechanical or electrical stimulation to induce ventricular premature contractions in patients in whom the heart was covered only by soft tissues.

A study was made to determine whether the rhythm produced was due to a reflex phenomenon or a direct mechanical stimulation of the

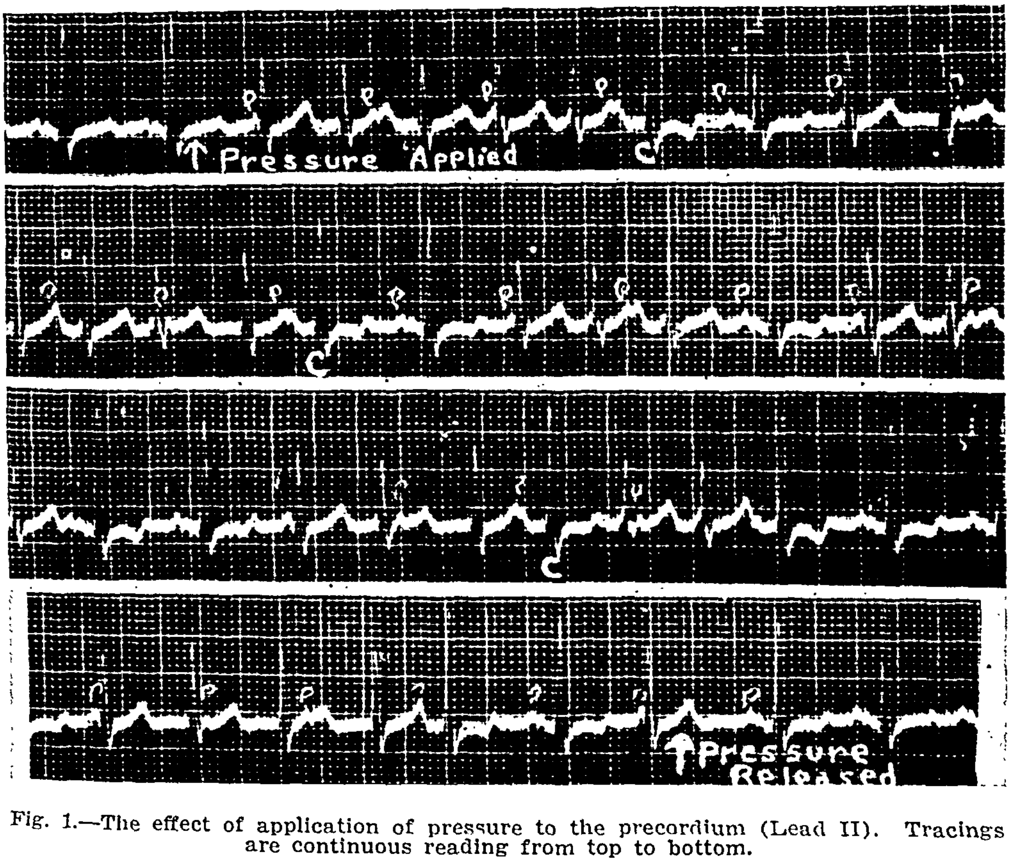

Fig. 1.—The effect of application of pressure to the precordium (Lead II). Tracings are continuous reading from top to bottom.

heart. The skin over the precordium was stimulated in various ways and electrocardiographic tracings were taken. The following methods were used: pinching and twisting, heating with a very hot water bag for twenty minutes, the application of faradic and galvanic currents, and superficial and deep thumb pressure. It was found that deep thumb pressure was the only effective stimulus and that the precordial surface was not uniformly responsive—the most irritable area being located at the third and fourth left intercostal spaces, about one inch from the sternum. Pressure applied within a radius of one inch from that spot would elicit the arrhythmia, but a proportionately greater

force was required as the distance from the center was increased. These observations suggest that the rhythm was not induced reflexly. To rule out any afferent pathway along the intercostal trunks, 2 per cent novocaine was injected to block the intercostal nerves from the anterior axillary line forward. Anesthesia was complete in the third, fourth, fifth and sixth intercostal spaces and partial in the second. Under these conditions deep pressure was quite as effective as before anesthesia. Under the fluoroscope a distinct costocardiac space was seen with the patient in the sagittal plane. When pressure was applied over the anterior chest wall and that space gradually obliterated, the tachycardia could not be induced until the chest wall came in contact with the cardiac shadow. These observations point to an action produced as a result of direct cardiac stimulation. Roentgen-ray and fluo-

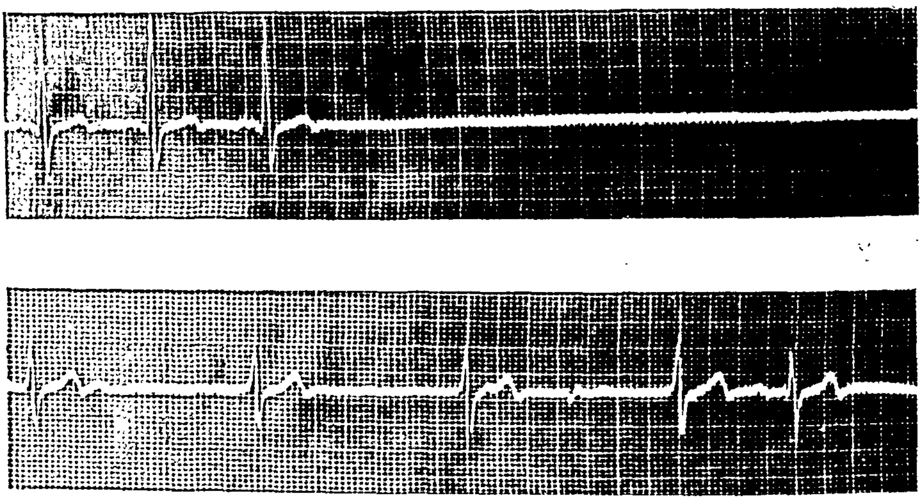

Fig. 2.—Effect of pressure on the eyeball (Lead II). Tracings are continuous reading from top to bottom.

roscopic studies place the most easily responsive precordial spot over a point between the left auricle and the left ventricle.

An attempt was made to determine what effect, if any, stimulation or depression of the vagus would have on the arrhythmia, and an effort was made to induce the arrhythmia in other ways than by pressure on the chest wall, such as exercise and the use of drugs—atropine, epinephrin, and digitalis.

Ocular pressure produced a marked bradycardia (Fig. 2), but pressure over the carotid sheath was ineffective. The slowing of the sinus pacemaker was so marked at times that ventricular escape occurred. If pressure over the precordium was applied simultaneously with ocular pressure, the ventricular rhythm was still produced, but with greater difficulty (Fig. 3). This points to some vagal control over the ventricular rhythm. Such a control in ventricular rhythm, particu-

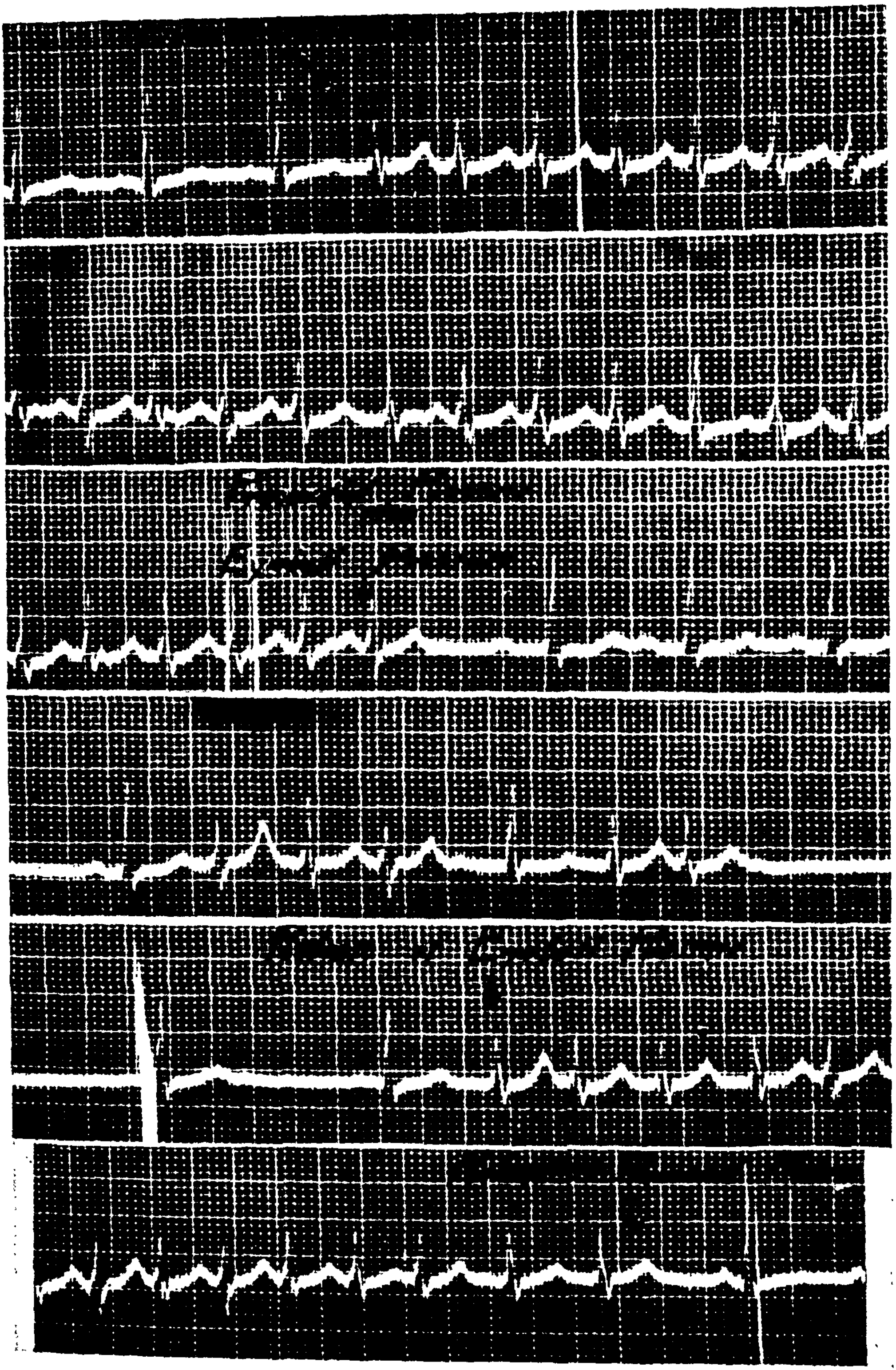

Fig. 3.—The effect of simultaneous pressure on the eyeball and the precordium (Lead II). Tracings are continuous reading from top to bottom.

larly in young patients, has been mentioned previously by Lewis.[5] Hewlett's case[3] shows the same phenomenon.

Since we have evidence that vagus activity may to some extent inhibit the production or maintenance of the ventricular rhythm, it was thought that paralysis of the vagi by atropine might cause the rhythm to be more readily induced. Atropine sulphate (3.0 mg.) was injected subcutaneously. A marked atropine effect occurred, including symptoms pointing to a central action. Sinus arrhythmia disappeared and ocular pressure became ineffective. The heart rate increased from 86 to 109. The rhythm remained of sinus origin, but precordial pressure could initiate the ventricular rhythm more easily than before the administration of atropine.

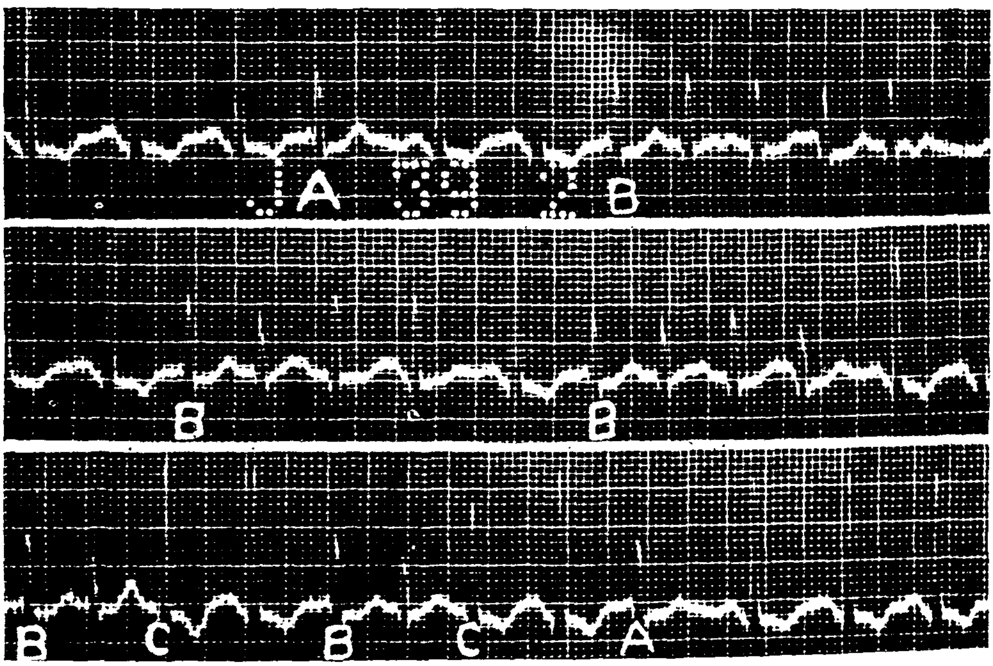

Fig. 4.—Spontaneous origin of the ectopic ventricular rhythm after the administration of atropine and adrenalin (Lead II). Tracings are continuous reading from top to bottom.

The next step was to determine the relationship of the sympathetic to the ectopic rhythm. Epinephrin chloride (1 c.c.) was injected intramuscularly (used in this instance as a sympatheticomimetic). The heart rate increased from 80 to 100 and the sinus rhythm was maintained. Just as with atropine the arrhythmia was produced much more readily than before the administration of the drug. The same observations were made on three different occasions. In order to obtain an epinephrin effect, unattended by vagus action, 3 mg. of atropine sulphate were injected subcutaneously, followed in 45 minutes by 1 c.c. of epinephrin chloride intramuscularly. The heart rate increased from 86 to 140, shortly after the injection of the latter drug. This high rate gradually decreased to 120 per minute at the end of four hours.

Within ten minutes after the injection of the epinephrin the ectopic ventricular rhythm developed spontaneously and thereafter occurred paroxysmally alternating with the sinus tachycardia. The spontaneous paroxysms were short, not exceeding fifteen beats, and in many instances only one ectopic beat would appear. These paroxysms gradually decreased in frequency, the last one observed occurring three and one-half hours after epinephrin was injected, at which time the sinus rate was 130 per minute.

Fig. 4 is an electrocardiogram, Lead II, showing spontaneous origin of the ventricular rhythm. At points *A* the normal sinus rhythm is interrupted by a single ventricular premature contraction, which is definitely premature and is followed by a compensatory pause. At points *B* the normal sinus rhythm is interrupted by runs of ventricular tachycardia. The ventricular premature contractions are exactly of the same type as those of the paroxysms. This, according to Robinson and Herrmann,[9] is suggestive of the ventricular origin of the tachycardia. It will be noted that the P-waves are independent of the ventricular rhythm, due to retrograde block, which is another evidence, according to the same authors, of the ventricular origin of the tachycardia. At points *C* are normal ventricular beats in response to auricular impulses interrupting the ventricular rhythm.

To rule out the possibility that rapid rate alone was responsible for the origin of the arrhythmia, tachycardia with rates exceeding 130 per minute was induced by exercise. The tachycardia so induced was not interrupted by ectopic beats.

The conclusions derived from these observations are that the vagus and sympathetic nerves are both able to influence the arrhythmia. Activity of the vagus prevents the spontaneous origin of the arrhythmias, and its stimulation inhibits the continuance of the ectopic rhythm once it is induced. Stimulation of the sympathetic increases the ease with which the ventricular rhythm is produced, and if at the same time the vagus influence is removed, it initiates the rhythm. The exact part these nerves play in the mechanism could not be determined. It is probable that their action is indirect, in that by decreasing or increasing the irritability of cardiac muscle they render the heart either less or more responsive to impulses emanating from the ectopic focus.

The effect of digitalis was investigated at two different periods, about one year apart. In neither instance was the pressure mechanism affected by the drug. The first investigation was made while the heart was easily responsive to precordial pressure. The patient was digitalized with a single dose of the powdered leaf, using 0.11 cat unit per pound body weight. The electrocardiograms showed many ventricular premature contractions of different origins. In some cases the ventricular premature beats came so early that they began on the T-wave of the preceding ventricular complex. The normal pacemaker was re-

placed by a wandering pacemaker, and there were a few single complexes which resemble those produced by pressure over the precordium. The second set of observations was made at a time when the heart was not readily responsive to precordial pressure. The patient was digitalized very slowly with the same preparation as used before, until there were definite signs of a mild toxicity. Daily electrocardiograms showed no changes except a few premature contractions. We could draw no inferences from these observations with respect to the effect of digitalis on the arrhythmia.

SUMMARY

1. A case is reported in which a rapid ventricular rhythm is produced by pressure over the precordium.

2. The stimulus appears to be a direct pressure effect on the heart, and not a cutaneous reflex phenomenon.

3. The ventricular rate is higher than the auricular rate (ventricular rate 170 per minute, auricular rate 80 per minute). The auricular rate is the same as that before the ventricular rhythm was produced and is in response to the sino-auricular node.

4. Forward conduction is unimpaired as shown by the appearance of normal ventricular complexes in response to the auricular beats which reach the ventricle when it is not refractory.

5. Stimulation of the vagus tends to inhibit the production of the independent ventricular rhythm.

6. Stimulation of the sympathetic when the vagus is paralyzed will induce the arrhythmia.

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ELECTROCARDIOGRAPHIC RECORD OF A PAROXYSMAL CARDIAC IRREGULARITY AS A MANIFESTATION OF THYROID ADMINISTRATION

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THE accompanying electrocardiogram shows a normal cardiac sequence in Leads I, II, and III, with a cardiac rate of approximately 100, until the last cycle illustrated on the third strip of tracing (Lead III). There it will be seen that the auricular rate has increased to 150 with the ventricles following irregularly. On the last strip the auricular rate approximates 400 to the minute, while the ventricular rate throughout this period is quite irregular but as a general rule approximates 150. In places the auricle may be fibrillating. Finally, in the sixth cycle from the end in the last strip the irregularity of the auricle suddenly ceases and the electrocardiogram resumes the picture seen before the attack started. In this transitional cycle there is a hiatus of a complete second between beats of auricle and ventricle; and, when normal mechanism is resumed, the auricle initiates the cycle.

This tracing was made of a patient forty-nine years old who is himself a professor of pharmacology. During the course of a hypertrophic osteoarthritis, it was found that his basal metabolic rate was minus 28 per cent, and he was given thyroid extract for several weeks without any alteration of either the metabolic or the pulse rate. Consequently the thyroid extract was stopped and he was given thyroxin by mouth, 0.8 mg. three times daily. His rate was brought to normal and maintained at normal on this dosage. During the course of this period he developed some edema that seemed most likely to be a manifestation of cardiac insufficiency, and he received tincture of digitalis, 3 c.c., daily until the edema disappeared and alterations were noted in the T-wave of his electrocardiogram.

Three weeks before this tracing was made it was noticed that the P-R time had increased to 0.20 second. Digitalis was discontinued and was not resumed again in the interval prior to the attack of paroxysmal cardiac irregularity which is depicted. While he was on digitalis, his vital capacity rose from 3171 to 3845 c.c. At this time his basal metabolic rate was plus 4 per cent, and he was taking 2.2 mg. of thyroxin daily. Two weeks before the attack noted his basal rate and vital capacity were again measured and were unchanged. On the day on which the tracing was made he had come for estimation of his basal rate, and it was found to be minus 3 per cent with a vital capacity of 4146 c.c. While he was dressing, his heart became a little

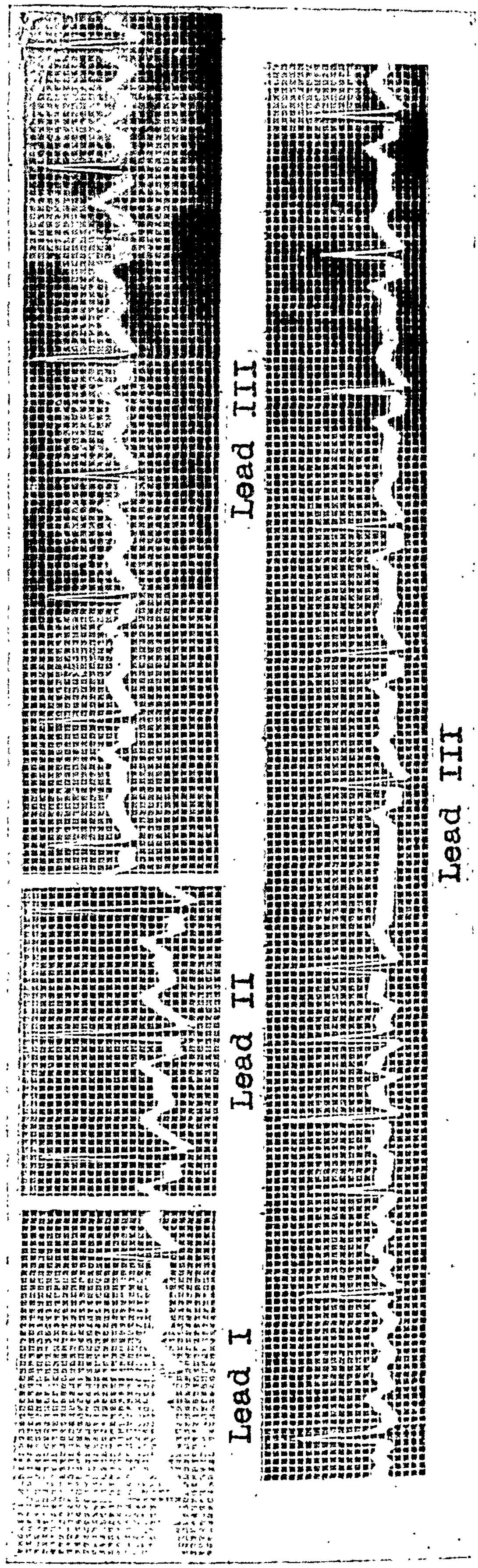

Fig. 1.

irregular and it was in that way that the accompanying tracing was obtained. The attack of irregularity lasted for two minutes; a complete record was obtained, but only the beginning and the end are shown here. He had had no digitalis for three weeks; and, though he was taking thyroxin, he had not taken a sufficient amount to elevate his basal metabolic rate above normal. As a result of this attack, the thyroxin was stopped for almost a month during which time he experienced no further cardiac attacks and his basal rate slipped back to plus 29 per cent with a basal pulse of 64.

The paroxysmal cardiac irregularity picture apparently occurred as a result of thyroxin administration, even though a sufficient amount was not given to raise the basal metabolic rate above the normal. The tracing itself is of importance in that it depicts (1) the transitional cycles between normal mechanism and the beginning of the irregularity and (2) the end of the irregularity and the resumption of the normal cycle.

Department of Reviews and Abstracts

Selected Abstracts

Morawitz, P.: Prevention of Sudden Deaths From Heart Disease. München. Med. Wchnschr. 76: 1075, 1929.

The author believes that in many cases it is possible to recognize disturbances in cardiac function which are very likely to lead to ventricular fibrillation and sudden death. Suggestive symptoms include anginal attacks, especially during rest, cardiac asthma, attacks of tachycardia, weakening of the apex impulse and a fall in a previously high blood pressure. Electrocardiographic changes include lengthening of the P-Q and Q-R-S intervals with arborization block, absolute arrhythmia, the Pardee wave and negative T-wave.

Believing that quinidine would be of value in preventing the onset of ventricular fibrillation, the author began in 1928 to give it routinely in all cases where he suspected this possibility. His results of 1928 are compared with control data in 1927.

	CONTROL 1927	QUINIDINE 1928
Sudden deaths	43	19
Compensated	24	5
Decompensated	19	14

He concludes that quinidine is of great value in preventing sudden deaths, especially in compensated arteriosclerotic and luetic cases, where the cardiac damage is not particularly extensive. He gives it for long periods of time in doses of 0.2 gm. daily and has observed no ill effects.

Fischer, Robert, and Kiss, Aristed: A Contribution to the Knowledge of Pararrhythmia. Deutsche Arch. f. klin. Med. 164: 73, 1929.

A case is presented of nodal rhythm alternating with cycles of normal sinus rhythm and occasional auricular extrasystoles. The cycles of normal rhythm always appeared after a definite interval following the previous nodal systole; and the successive cycles showed an increase in time interval, although at the same time there was a decrease in conduction time. The explanation for this increase in time interval is not quite clear.

Haag, Harvey B., and Hatcher, Robert A.: The Stability of Digitalis and Its Preparations. J. A. M. A. 93: 26, 1929.

Six specimens of powdered digitalis have been examined after intervals varying from one to sixteen years, and in no case has deterioration been detected, and the authors believe that no one working in their laboratory has ever observed anything indicative of deterioration in one of the many specimens of powdered digitalis used. Powdered digitalis in capsules or in tablets is admirably suited for securing uniformity of doses where individual patients, clinics or groups of clinics are provided with sufficient amounts to last one year or more.

A sterile infusion of digitalis undergoes little change within several months, and deterioration then results solely in diminished activity, not in increased toxicity.

The offical tincture of digitalis retains its activity with comparatively little change during the several years, and any change that does occur merely calls for a corresponding increase in dosage. The secret of deterioration of liquid preparations has not been explained fully, and there is no evidence that any of these preparations are as stable as powdered digitalis kept with ordinary care in a corked glass bottle.

Aqueous solutions of strophanthin, ouabain or other digitalis principles, kept in ampules of soft glass deteriorate rapidly. Ouabain solution in ampules of hard glass decompose slowly. There is no evidence that any of the digitalis specialties in use are more stable than the official digitalis tincture.

Schwartz, Sidney P. and Weiss, Morris M.: Digitalis Studies on Children With Heart Disease. The Effects of Digitalis on the Electrocardiograms of Children With Rheumatic Fever and Chronic Valvular Heart Disease. Am. J. Dis. Child. 38: 699, 1929.

A summary of the results obtained from the administration of a single body-weight dose of digitalis to 24 children with chronic rheumatic valvular heart disease and signs of heart failure reveals that the use of the drug by this method is a safe procedure in children exhibiting sinus rhythm or an irregular ventricular rate due to auricular fibrillation. There were no untoward symptoms from the administration of the drug in a single dose of this type provided it was well diluted with water.

The changes induced by the drug were recorded in 12 of 18 children with sinus rhythm and in 5 children with auricular fibrillation who were studied during both the active and inactive phases of rheumatic fever. The alterations produced on the electrocardiogram consist essentially of a lowering of the S-T segments below the isoelectric line with final progressive increases in the negativity of the T-wave in one or more of the leads in which it was previously upright. In 2 children a previously negative T-wave in Lead III eventually became positive. In 6 of the eighteen children no electrocardiographic signs of digitalis action were observed.

A transitory slowing of the sinus rate of between 10 and 15 beats per minute in 12 children with sinus rhythm and a reduction of the ventricular rate in auricular fibrillation from an average of 157 beats per minute to 60 beats per minute within twenty-four hours was observed following the dose of digitalis. In one child the administration of digitalis augmented the size of the P-R interval during an attack of rheumatic fever.

The inconstancy and variability of the appearance and duration of the changes induced by body-weight doses of digitalis on the S-T interval and T-waves of the electrocardiograms of children make this method of studying the doses of digitalis in children totally inadequate. For similar reasons, the effects of digitalis on the electrocardiograms of children cannot be taken as criteria in measuring the standardization of the drug, its rate of absorption and elimination or the daily amount necessary to maintain its persistent effects known as the maintenance dose.

Cloetta, Max: The Biochemical Action of Digitalis. J. A. M. A. 91: 1463, 1929.

The author in this article discusses briefly his conclusions as to the action of digitalis preparations on the heart muscle from a pharmacological standpoint. He presents certain conclusions that are of a clinical nature. He believes that digitoxin has a more important and a more lasting effect on the heart muscle than any of the other derivatives from folia digitalis. From a study of the mechanism of cardiac response, he believes that under the influence of digitalis the cardiac muscle is

capable of overcoming a greater resistance without having to undergo dilatation. In studying animals with experimental valvular lesions of the heart, he has found that if digitalis is administered to these animals immediately after the aortic defect develops and the treatment is regularly continued, then the dilatation and hypertrophy never reach the high degree attained without digitalis treatment. When these aortic deficient hearts are compared with normal hearts as to their absolute reserve energy, one finds that the crippled digitalis-treated heart is almost equal to a normal one while the defective heart without digitalis treatment is much more rapidly exhausted. He believes that this should be sufficient to induce prophylactic treatment with digitalis in all early cases of endocarditis which are apt to terminate in valvular lesions.

A further discussion of the mechanism of digitalis action is presented. The author believes that digitalis has both fixed and reversible actions on the heart muscle, that is, certain derivatives, particularly digitoxin, become fixed in the heart muscle cells in such a way that it cannot be released by any physical process.

The relationship of calcium and calcium therapy to digitalis is fully discussed.

Harvey, E. Newton: The Effect of High Frequency Sound Waves on Heart Muscle and Other Irritable Tissues. Am. J. Physiol. 91: 284, 1929.

High frequency sound waves of high intensity will cause rhythmic contraction of quiescent ventricular muscle of frog or turtle immersed in Ringer's solution and a more rapid natural rhythm of the auricles accompanied by lessened amplitude of contraction and often by increased tone. Touching ventricle or skeletal muscle or nerve to glass carrying intense supersound waves does not stimulate, but nerves and skeletal muscle of frog or turtle containing nerves show a few subminimal twitchings of short duration when immersed in Ringer's solution. The effect may be due to increased pressure changes accompanying the sound waves, since it is known that increased pressure will stimulate.

Schneider, Edward C., and Ring, Gordon C.: The Influence of a Moderate Amount of Physical Training on the Respiratory Exchange and Breathing During Physical Exercise. Am. J. Physiol. 91: 103, 1929.

Following a study of the effects of moderate physical training on the basal respiratory exchange, pulse frequency, and arterial blood pressure, the authors have studied the changes in the position of the "crest-load" in the respiratory exchange and in the minute volume of breathing for two subjects while performing physical work through a period of regular physical training and during an after period when no exercise was taken in order to determine how soon and to what extent moderate regular exercise may influence each.

The percentage of carbon dioxide in the expired air of a work period has been used to determine the amount of work that constitutes a "crest-load"; so long as the percentage of the exhaled carbon dioxide rises proportionately with added increments of work the load is considered normal. The crest-load is reached when the oxygen-supplying mechanisms working at full capacity just meet the oxygen need of the reconversion process of the muscles. With this load the percentage of exhaled carbon dioxide is at its maximum. A further increase in the load of work becomes an overload and is associated with the escape of lactic acid from the muscles into the blood and a proportionate reduction in the formation of carbon dioxide. When this occurs, the percentage of carbon dioxide in the exhaled air is less than it is with the crest-load.

Moderate physical training, about an hour daily, increased the load-carrying ability within one week in the subjects studied, but the full effects were only ob-

served after five to seven weeks. Any let-down in the regularity or amount of daily work soon reduced the load-carrying ability, but even with complete neglect of exercise some of the gain in power was maintained for several months. The percentage of carbon dioxide exhaled and of oxygen absorbed during work is increased by training, the full effects being reached within four or five weeks. These soon drop back to the pretraining level when training is discontinued.

The minute volume of breathing for any given load of work decreases with training and reaches its lowest level in from four to six weeks. This effect disappears within four to six weeks after training changed overloads to normal or crest-loads. In one subject the absorption of oxygen was increased as training changed overloads to normal or crest-loads. In another subject a slight decrease in the oxygen consumption of work was evidenced as training proceeded. A decrease in the respiratory quotient of work during training suggests a gain in ability to reconvert lactic acid more adequately into its precursor.

Simpson, R. H., and Batten, Lindsey W.: Some Points in the Diagnosis of Cardiac Lesions in Children. Lancet 2: 372, 1929.

An attempt has been made to indicate the main differences between child and adult cardiology and to point out some of the problems peculiar to children and how they may be faced.

The diagnosis of fully developed lesions is on the whole easier in children than in adults and even prognosis is in some respects less difficult than it becomes after middle life but the problem of the early developing lesion is at times one of the greatest difficulties. To form an opinion on the state of the heart at the moment of examination may not be hard, but there will arise the question "is this heart the seat of active infection—is this slight abnormality the first sign of serious trouble?" To answer this question a thorough and general investigation of the child and his history will be necessary, and in some cases a period of observation while the diagnosis remains in doubt cannot be avoided. Such cases are, however, the exception and not the rule. In very many cases brought up for decision the diagnosis of "healthy heart in a healthy child" can be made with confidence. In another group, the nature and degree of cardiac damage can be stated with reasonable certainty, the present infection excluded, a suitable regimen instituted and a watch kept for any recurrence of active trouble. In doubtful cases the necessity for reaching a decision at the earliest possible moment should never be forgotten.

The insidious nature of the rheumatic infection and the variation of its manifestations has lately been emphasized. Parents, teachers and others responsible for the health of children should take early and serious notice of fidgetiness and joint pains, fever and tonsillitis. The doctor knowing well the damage rheumatic infection can do is tempted to an attitude of extreme caution. This is from one point of view amply justifiable. It must be remembered that while childhood is the time when rheumatic infection does its worst, it is also the time when accidental and insignificant murmurs are commonest and the pulse rate most variable and easily disturbed, and furthermore, it is the time when character and emotional outlook are being formed. Six months of rest in bed to recover from cardiac dilatation may prove to be invested soundly: six months of doubt and caution with restrictions of play and exercise in an atmosphere of anxiety are unlikely to stay the progress of an insidious carditis but are well calculated to sow the seeds of a cardiac neurosis difficult or impossible to eradicate.

Hooker, D. R.: On the Recovery of the Heart in Electric Shock. Am. J. Physiol. **91:** 305, 1929.

A new method based on physiological principles for the recovery of the heart in electric shock is described, and the results from its use are reported. This method although complicated and difficult of practical application seems, as judged from the results obtained, to promise a real advance in control of ventricular fibrillation.

Ventricular fibrillation is believed to be the most common cause of death in electric accidents. In the dog, as is assumed to be the case in man, ventricular fibrillation when once established is all but invariably permanent with resultant death, since the fibrillating ventricles are incompetent to maintain the circulation.

Potassium chloride is the only agent of demonstrated efficacy in overcoming ventricular fibrillation. It acts by producing a state of inhibition. This inhibition, in turn, can be overcome by removing the excess potassium from the coronary vascular bed.

With these facts in mind, experimentation led to a procedure suitable for the resuscitation of dogs in which ventricular fibrillation had been induced by electric shock. This procedure calls for the central carotid injection of the remedial solutions, saturated with oxygen and warmed to body temperature. The first solution of potassium chloride 0.5 per cent, sodium chloride 0.9 per cent, and heparin 0.25 mg. per c.c. establishes potassium inhibition, and the heart is allowed to rest for one minute. The second solution, calcium chloride 0.025 per cent and sodium chloride 0.9 per cent, washes the excess of potassium out of the coronary bed and substitutes a relative excess of calcium chloride, the effect of which is to stimulate a normal cardiac rhythm. This effect is enhanced by the coincident injection of 1 c.c. of 1:1000 adrenalin chloride.

The author states that such an approach to the problem of resuscitation from ventricular fibrillation has not heretofore been suggested and it has resulted in a number of spectacular recoveries. The method should, however, be subjected to further critical study before considering its application to man because there are obvious indications that it may be improved, particularly for use in cases of long-lasting fibrillation.

Veil, W. H.: Rheumatic Infections. Deutsche Med. Wchnschr. **55:** 556, 1929.

The author holds that rheumatic fever may primarily involve the renal glomeruli, causing an acute or chronic glomerulonephritis. The subsequent development of typical migrating arthritis or of endocarditis gives a clue to the renal picture. In two cases with uremic manifestations, very marked improvement occurred following tonsillectomy.

Not only the renal glomeruli but the renal capsule likewise may bear the brunt of a rheumatic infection. The author uses the term perirenitis; and cites a very interesting case. This was a patient forty-five years old, with rheumatic pericarditis and a diminished urinary output, who had been under treatment with salyrgan and strophanthin for the relief of edema. A tumor the size of a child's head was found in the position of the right kidney, and a markedly diminished secretion was obtained from this kidney on ureteral catheterization. At the exploratory operation there was found a large spongy sac consisting of loose connective tissue in the depths of which a small discolored kidney was embedded. After splitting the kidney capsule proper, the kidney immediately assumed its normal size and color. Directly thereafter, the urinary output became normal.

Graham, Evarts A.: Decompression of the Heart. Ann. Surg. 90: 817, 1929.

The purpose of the paper is to record two cases in which operation was performed for the deliberate purpose of decompressing the heart. The principle of this decompression is likened to that of decompressing the brain or thorax when there is present increased pressure within the cavity. The author discusses the question of the heart that may be embarrassed by confinement within a bony chest wall apart from whatever embarrassment may result from restriction of its movements by pericardial adhesions. In the two cases reported, the pericardium was not thickened and in the second case, no adherent pericarditis was present. Both cases had suffered from periods of cardiac decompensation and embarrassment and showed a very marked enlargement of the heart. Following thoracoplasty over the precordium, both patients obtained marked subject improvement. In the second case there was objective disappearance of a raised venous pressure and nodal rhythm which had been present before. Both patients lived several months after the operation in comfort until they died, the first of an acute pulmonary infarct, and the second of acute pneumonia.

Dickson, D. Elliot, and Dickson, W. Arnott: Arteriosclerosis in Coal Miners. Brit. M. J. 2: 1103, 1929.

The results of a consecutive examination of the circulatory system of 500 coal miners are studied. It is shown that among coal miners of all ages there is an extraordinary prevalence of thickened arteries; the thickening is confined to the intima in the specimens examined. There is no associated rise in blood pressure. There is an unexplained difference in the mortality rate of coal miners as compared with other males.

Of the 500 individuals examined, 116 were twenty years or under, 180 were twenty-one to thirty years; 111, thirty-one to forty years; 61, forty-one to fifty years; 32 were over fifty years of age. Of 500 miners examined only 44 had arteries which could not be palpated. These occurred principally among those individuals under thirty years of age. Two individuals, both of whom were over fifty years of age, had arteries so thickened as to be classified as atheromatous. These showed marked calcareous degeneration. After the age of forty years, none of the men had arteries which were not palpable. Four hundred forty-nine cases out of 500 had blood pressure falling within normal limits, and only 51 showed blood pressure over 140. It is suggested that the arteriosclerosis shown to exist in coal miners is the explanation of the peculiarity in their mortality rate. In an attempt to explain the reason for this arteriosclerosis, the authors have found that the only significant constant factors are: (a) the inhalation of air of altered composition, especially the CO_2 content; and (b) the absence of daylight.

Robertson, H. F.: Vascularization of the Thoracic Aorta. Arch. Path. 8: 881, 1929.

Following the suggestion of Klotz that the localization of syphilitic lesions in the ascending aorta might have an anatomic basis, the author has studied the vascularization of the thoracic aorta. The hearts of dogs, lambs and human beings were injected by aortic cannulas so that the first coronary branches which gave vessels to the aorta were always filled. Radiography, dissection of cleared and uncleared specimens, and corrosion of specimens were carried out. Serial sections gave the details of the distribution of the vasa vasorum and other fine vessels.

From the data furnished by these experiments, the thoracic aorta may be roughly described as vascularized by a sheath of areolar connective tissue richly supplied with blood vessels. Over the arch and the descending thoracic limb, this sheath

contained at least two distinct layers of interweaving vessels which were derived from vessels of adjacent structures or from branches of the aortic efferent vessels. Over the ascending limb, only a single network was usually seen, derived from coronary branches from cardiac fat-pad branches of these and from descending vessels of the aortic arch. At the root of the aorta, the richest vascular bed was found.

The author believes that the blood vessels are found to be most numerous in the aortic wall where aortic disease other than senile change is the most commonly localized. A relation exists between the presence of certain lesions of the aortic wall and the distribution of the vasa vasorum.

Semsroth, Kurt, and Koch, Robert: Studies on the Pathogenesis of Bacterial Endocarditis. Arch. Path. 8: 921, 1929.

In human endocarditis, the earliest endocardial change has until recently generally been supposed to be an "endothelial damage" preceding the localization of bacteria. This endothelial damage has never, however, actually been observed. Mononuclear endocardial cell proliferation, on the other hand, is a well-known constituent of human endocarditis. Autopsies on several patients who showed early endocarditis showed the authors the possibility of studying early endocardial reactions in endocarditis. In these patients nodular monocytic proliferations were not infrequently observed underneath an intact endothelium and far from the site of thrombotic deposits. This observation allows the conclusion that monocytic endocardial proliferations in human endocarditis are *not* invariably the sequel of thrombotic deposits. Furthermore, in several mononuclear endocardial cell proliferations, areas of transformation of the intercellular substance into hyalin were found associated with a defect of the surface endothelium but without a thrombotic deposit. The authors infer that these cellular proliferations may arise in the absence of thrombotic deposits and may through regressive changes develop endocardial defects which in turn may become the site of thrombi.

In other words, nodular mononuclear cell proliferations of the human endocardium may precede the formation of morphologically detectable endocardial defects and endocardial thrombotic deposits.

In studying the reactions of animals to protein sensitization for other purposes, the authors have noted similar nodular mononuclear cell proliferations; and they, therefore, raise the question as to whether or not these processes may not be somewhat related to the sensitization processes of human rheumatic fever. This inference that bacterial localization on the endocardium results from its altered capacity to react toward bacteria would seem logical. This relationship, however, is scarcely true within the confines of specificity as the "allergic state," so-called may be induced by a nonbacterial foreign protein.

Ceelen, W.: Present Status of Myocardial Lesions. Deutsche med. Wchnschr. 55: 569, 1929.

The author briefly discussed the common pathological lesions of the myocardium. He calls attention to a peculiar type of myocarditis occurring in children in the first two years of life, often associated with status lymphaticus. The following case is cited as an example: A child, five months old and previously well, became ill suddenly and died within twenty-four hours. The ventricles of the heart were enlarged, and an extensive lymphocytic infiltration was found in the myocardium, causing considerable destruction of the muscle fibers. Although this lymphocytic infiltration might be considered as the accompaniment of a status lymphaticus, the author favors an infectious origin.

Fahr, Th.: Cystic Kidneys as a Cause of Constant Hypertension. Deutsche med. Wchnschr. 55: 572, 1929.

The author believes that cystic kidneys can cause cardiac hypertrophy and hypertension only which the kidney parenchyma is seriously involved.

Dietlen, H.: Problems in the Pathology of the Circulation. Deutsche med. Wchnschr. 55: 566, 1929.

The question is raised whether in certain disturbances of the circulation the capillary function may not be primarily involved, with secondary cardiac embarrassment. The rôle of the capillaries in the control of the return circulation to the heart is evident from: 1. The ability of the spleen and the subpapillary dermal plexuses to act as reservoirs of large quantities of blood, said at least to be one liter. 2. Variations in the size of the capillary vessels as a result of changes in the hydrogen-ion concentration of the surrounding tissues.

The author suggests that one should look for capillary disturbances in cases refractory to digitalis.

Lundy, Clayton J., and Woodruff, Lewis H.: Experimental Left and Right Axis Deviation. Arch. Int. Med. 44: 893, 1929.

Using a method previously described by the authors of placing and distending a balloon in various chambers of the heart and in the great vessels, electrocardiographic evidence of right, and left axis deviation was studied. The method permits electrocardiographic observation of the effect of increased pressure within and distention of the cardiac cavities and of obstruction to blood flow in the great vessels of the intact young dog under light ether anesthesia. Several undesirable features of the method of study are discussed in this paper. The desirable features are that the method may be used on the intact dog, that complete recovery occurs enabling one to repeat the experiments many times on the same dog. It is also possible to influence separately either the right or the left ventricle.

Acute dilation of the right ventricle was produced with corresponding right axis deviation. The authors then discuss the possible factors in these experiments for the production of axis deviation and various arrhythmias of the heart. They state that stretching of the muscle cells of the individual ventricles produced directly by the balloon or distention with blood may cause increased permeability of the cell membranes, thereby increasing the excitability of that individual ventricle with corresponding electrocardiographic evidence of axis deviation. They also believe that the lowered resistance produced in this manner between the individual cells may account for a small part of the axis deviation. Another explanation may be that partial asphyxia may cause an increased permeability of the cell membranes or may change the character or concentration of the electrolytes contained within the cells making them more diffusible.

Other possible explanations are: (1) The rate of propagation of the action current may be increased; (2) there may be a change in the direction of the action current associated with a change in the direction of the nerve fibers caused by distention with the balloon; (3) there may be a change in the relative volume or mass ratio between the left and the right ventricles; (4) factors of decreased as well as increased excitability may be present. The possible importance of these and similarly acting factors as a mechanism for clinical changes of the electrocardiogram is discussed.

Hartman, Howard R., and Ghrist, David G.: Blood Pressure and Weight. Arch. Int. Med. 44: 877, 1929.

This study has been undertaken for the purpose of determining the relationship, if any, that exists between arterial blood pressure and body weight. To obtain the data for this study records of 2,042 consecutive registrants fifteen years old or more were taken from the files of The Mayo Clinic for June, 1927. Nine hundred and fifty-nine of the subjects were males and 1083 females. By use of the Nylic standard table of heights and weights, percentage deviation from normal weight was computed in each case. The arrangement of groups by percentage deviation from normal was then accomplished for males and females.

In the charts there is shown in males an almost step-like rise from the group 26 to 50 per cent underweight to the group 51 to 75 per cent overweight in the mean values for the systolic blood pressures of the groups. The most significant rise of systolic blood pressure is demonstrable between normal weight and 11 to 25 per cent overweight. The marked difference between the total underweight and the total overweight male groups is strikingly significant. In the female group there is a similar step-like rise in the systolic blood pressure. The marked difference between total underweight and total overweight between groups is practically as striking and is equally as significant as it is in the males.

Hartman, Howard R., and Brown, George E.: The Systolic Blood Pressure in Duodenal and in Gastric Ulcer. Arch. Int. Med. 44: 843, 1929.

This study was undertaken to determine whether or not patients suffering from duodenal or gastric ulcer have low systolic blood pressures. The data were compiled from the records of patients with duodenal or gastric ulcer examined in The Mayo Clinic by a diversified group of internists. Thus multiple personal equations are expressed in the readings which were taken without the subject under consideration in mind. The readings were recorded immediately on a history sheet, and from these records the charts were compiled and curves constructed by a statistician, who had no knowledge of the preconceived hypothesis. The calculations and mathematics of biometry were checked throughout by other statisticians. The first series of cases studied comprises 865 of duodenal ulcer and 561 of gastric ulcer. In selecting the patients, the question of whether blood pressure was normal or abnormal was not considered. The series included cases of severe hypertension due to independent conditions associated only by coincidence. The data were corrected for age and weight against 1016 cases encountered in the routine of work at the clinic.

In order to make the comparison fairer, three additional groups were studied. One of these comprised 1,685 cases of cholecystitis. In 782 cases in this group cholelithiasis was present. The second of the three additional groups to undergo analysis was made up of 571 cases of inoperable carcinoma of the stomach and 239 cases of carcinomatous gastric ulcer. The third additional group was made up of cases, the reports of which were obtained from one life insurance company. The "normal blood pressure curve" that was used by the company was not included, but derived averages of calculation from the frequency distribution of the various blood pressures in five-year age groups of all persons who applied for life insurance during a given period were taken as the curve for comparing with the other groups.

The blood pressures in cases of duodenal and gastric ulcer compared with the curve constructed from life insurance statistics are lower in men and in the sexes combined, but are not lower in the females alone. Too much stress, however, cannot be placed in this comparison because of the fact that the insurance cases were not corrected for weight and the other groups were not corrected against a

normal blood pressure but against a control group. The blood pressures in this control group also are higher than those in the ulcer group in both males and females, but the variation is not of significance. The curves remain fairly parallel throughout all ages.

In comparing the blood pressure in cases of duodenal and gastric ulcer with that in cases of cholecystitis and carcinoma of the stomach or carcinomatous ulcer, the difference is not significant in either males or females.

Major, S. G.: Blood Pressure in Diabetes Mellitus. Arch. Int. Med. 44: 797, 1929.

Blood pressure in a clinical series of 500 cases of diabetes mellitus is compared with the blood pressure in three control groups. The first control group consisted of 356 dispensary patients, all of whom were thirty-five years or older. In the second control series, the blood pressures in 472 consecutive hospital cases were studied. These cases as well as those in the former group were taken regardless of the complaint of the patient. In the third control series blood pressures were taken on apparently normal persons. In the 500 clinical cases of diabetes mellitus, 408 were thirty-five years or older. The figures obtained from the study are subjected to a statistical analysis.

In elderly diabetic patients, systolic blood pressure is slightly higher than that of patients seen in a dispensary series or in a hospital series and considerably higher than the blood pressure in normal persons of the same age group. Although the mean systolic blood pressure in the diabetic series is not essentially different from that in either the dispensary series or the hospital series, there is a greater tendency to a slight elevation of the systolic blood pressure in diabetic persons than in those in the other series mentioned, as is shown by a statistical study.

In a study of 104 cases of diabetes mellitus coming to post-mortem examination, all cases showing vascular injury were excluded. In the remainder, after calculating the mean weight, according to sex and also according to five-year age groups, it was found that the weight of the heart of the men in the diabetes series exceeded that of the men in the control series after the fifty to fifty-five years of age group; whereas the weight of the heart of the women in the diabetic series exceeded that of the women in the control series after the age of sixty-five to seventy years. When both sexes were included in this comparison, it was found that the curve representing the diabetic series was higher than that representing the control series after the age of fifty to fifty-five years. It was found that the kidneys in the diabetic series weighed slightly more than those in the control series.

Pardee, Harold E. B.: Experiences in the Management of Pregnancy Complicated by Heart Disease. New York State J. Med. 29: 267, 1929.

Whether or not to allow a woman with heart disease to go through pregnancy depends on a prognosis. This prognosis depends upon the functional cardiac diagnosis, and this depends upon the patient's ability to perform physical exertion rather than upon the pathological state of the valves or myocardium. MacKenzie pointed the way to a better understanding of the problem by focusing attention upon the symptoms and signs of failure of the heart to maintain a normal circulation rather than on a diagnosis of an anatomical lesion. This report is based on the results in 106 patients in the antepartum clinic of the Lying-In Hospital, New York, from July, 1923, to July, 1925. Two of the patients had congenital cardiac abnormalities, one a patent ductus arteriosis. The others all had rheumatic heart disease. Mitral insufficiency was diagnosed in 29 patients; mitral stenosis in 64 and aortic insufficiency in 11, 3 of whom had also some degree of mitral stenosis. The patients

were classified according to the nomenclature adopted by the New York and American Heart Association. In Class I, there were 75 patients; in Class IIa there were 20, and in Class IIb there were 11. Six other patients admitted to the hospital during labor with heart disease in a seriously decompensated state belonged to Class III. Three of these patients showed pulmonary edema. The author believes that this functional classification serves as the best means for handling women during pregnancy. He believes that cardiac enlargement is not a reliable guide, since several patients showed marked degrees of enlargement without signs of compensation during labor. The prognosis will depend a great deal on the type of labor that ensues. When this is short in the first and second stages, the outcome will be favorable. He believes that the obstetrician should determine in each instance what measure should be adopted to hurry up safely the duration of labor.

In the antepartum clinic, the best treatment of these patients is the prevention of severe cardiac failure, and this means keeping watch during pregnancy for the appearance of increasing cardiac difficulty, appropriate treatment of the heart as soon as this is discovered, and interruption of pregnancy if the heart fails to respond to treatment after two or three weeks. In these patients cesarean section was performed on several occasions and seemed to produce very little strain on the heart. The results are better than from hysterectomy. Gas anesthesia during labor or during operation should be avoided, since it produces cyanosis and increased strain on the heart. Ether or chloroform were well tolerated. In this series of patients deaths occurred only in Class IIb and III. One patient in Class IIa died of pneumonia after operation, but there was no apparent effect from the heart.

The author concludes that Class I patients will not be in trouble during pregnancy or delivery under proper care, that Class IIa will probably not give trouble, that Class IIb will probably give trouble, and that Class III is a very difficult group to handle safely and that in this group the mortality is very high.

Levine, Samuel A., and Walker, George L.: Further Observations on Latent Hyperthyroidism Masked as Heart Disease. New Eng. J. Med. 201: 1021, 1929.

Attention is drawn to a group of patients usually treated for heart disease in whom the underlying cause is a latent and unrecognized hyperthyroidism. These cases are generally overlooked, for the common signs and symptoms, exophthalmos and thyroid enlargement, usually found in typical exophthalmic goiter and toxic adenoma are not evident in these patients. The diagnosis is even more difficult in patients who have coexisting organic heart disease such as angina pectoris, hypertensive heart disease or mitral stenosis. Of special interest are those with typical anginal attacks in whom proper treatment of the latent hyperthyroidism results in a great reduction in the number of attacks if not complete relief from symptoms.

The diagnostic criteria are discussed, and attention is especially directed to certain points in the general appearance of the patient, and in the physical findings which lead one to suspect the presence of a latent hyperthyroidism. These minor features are: periods of inexplicable diarrhea, unexplained loss of weight, nervousness, tremor, sweating and a feeling of warmth. Palpitation, shortness of breath, precordial pain and muscular weakness are of course common complaints, but they occur just as well in heart disease without as with hyperthyroidism, and therefore are not particularly distinctive.

Circulatory insufficiency is not a contraindication for surgery in the treatment of these patients, many of whom are relieved completely and others much improved by subtotal thyroidectomy.

A series of eleven cases is reported, all of which had been treated for a considerable period of time for heart disease, but in each of which there was a

latent hyperthyroidism either as the sole cause of the trouble or present as an additional burden on the heart already affected with some other organic lesion. One unusual case is included in this group in which there were associated attacks of synocope due to heart-block. Following subtotal thyroidectomy the attacks disappeared, and the patient has been much improved following the operation.

Dedication to Professor Wenchebach. Wien. Arch. f. inn. Med. 18: 1, 1929.

Professor Wenchebach's tenure of office as professor of medicine being terminated, he has been celebrated by a special issue of his paper, "Wiener Archiv für innere Medizin." V. Falta has edited and dedicated the volume which contains contributions from twenty-four of Wenchebach's students. The greater part of the volume contains cardiological papers. A long paper by Falta on renal diabetes and diabetes mellitus forms a notable exception.

Hans Kutschera Aichbergen (page 209) has written on cardiac asthma. He finds that in many cases of vascular failure the defect lies in the cardiovascular system itself rather than in extraneous factors such as anemia or too great demands by the organism. Among cardiovascular causes cardiac weakness in itself forms an important factor, and this has been made the subject of investigation.

In the early stages cardiac weakness can well be treated by rest and digitalis, later it becomes increasingly refractory to treatment until at last permanent failure sets in.

To explain the pathology he finds it useless to consider permanent cardiac damage, but it is necessary to look for such changes as are reversible when treated with rest and digitalis. In many cases the conditions which lead to cardiac decompensation correspond closely to the process of fatigue which occurs in any muscle.

Therefore, in cardiac weakness we are dealing with nonspecific fatigue phenomena, characterized by chemical and physicochemical changes, most important among which are changes in the concentration of the substances furnishing energy and increase in the permeability of the muscle cell membranes; that is, changes in the colloid phases. In cardiac as in other muscles the main changes occur in the phosphatides, which are decreased everywhere in the decompensated heart. Digitalis therapy was found to increase the phosphatides.

In cardiovascular insufficiency of infections not only the heart but muscle of the entire cardiovascular system is weakened. In these cases the heart muscle is found to suffer in a manner similar to that of chronic heart failure. This increased fatigability in infections is explained by suprarenal damage, for in the suprarenals as in the heart muscle, the damage is manifested by decrease in phosphatides. This is particularly interesting because it is related to muscle fatigue generally. This finally leads the author to a hypothesis of cardiovascular asthenia in infectious diseases as having their origin in suprarenal insufficiency.

Erich Zdansky (page 461) contributes a paper on pulmonary stasis in cardiac disease. The study is on the basis of roentgenological, clinical and anatomical investigations. In chronic congestion the lymph vessels of the interstitial tissues are dilated and the mediastinal lymph glands enlarged; this is mostly due merely to transudate, though infection seems to play a part in the enlargement of the hilus glands.

The edema is not evenly distributed throughout the lung but prefers the connective tissues around vessels and bronchi, especially in their bifurcations and their central parts. Probably this is due to diminished respiratory movements, and this makes absorption more difficult.

These factors, increase of lymphatic structures and uneven distribution of fluid in the lungs explain together the roentgen picture. The vascular pattern becomes

widened and increased, the hilus shadows become enlarged and indistinct, and indistinct ''flocculi'' are formed in the pulmonary fields.

In the x-ray picture may also be seen circumscript accumulations of transudate inside the lung; these are without relation to vessels and bronchi. They may be localized in areas and may occupy a lobe or an entire lung field. The pathogenesis of some of these is known as hypostatic pneumonia in dependent parts of the lungs.

But there are other, so far unknown, causes of these circumscribed areas of edema; indurations of lung tissue, caused by decreased respiration or anatomical narrowing of efferent lymph vessels. Tuberculous or anthrocotic changes in hilus glands may obstruct the drainage of transudate. Pleural adhesions may decrease respiratory movements with stasis resulting.

The clinical results of this uneven drainage will be a tendency to asymmetrical bronchitis, areas of consolidation and predisposition to pulmonary edema. In the roentgen pictures these lesions may often appear as focal pulmonary infiltrations, miliary disseminations, extensive pneumonic processes, infarcts, etc. A differential diagnosis from these lesions may be difficult. The swelling of the hilus glands may become so extensive as to become visible on the roentgen pictures, where they appear with indistinct margins owing to the general moisture of the lungs. Pleural adhesions may often be diagnosed by edematous infiltrations.

The problem of coronary thrombosis is attracting attention also on the continent. Richard Singer, p. 421, in this volume describes its ''Clinic and Therapy'' on the basis of 20 cases. The symptoms are: pain of the angina pectoris type, not relieved by nitroglycerin, and fever. If the left ventricle is affected, left ventricular insufficiency is indicated by Cheyne-Stokes breathing. Electrocardiographic disturbances occur in almost all cases; during the first forty-eight hours, the findings are typical, after this many variations may occur. Most commonly there is an isoelectric, diphasic or negative T-wave, widening or splitting of the R-wave; frequently the Q-wave is remarkably deep. Tachycardia, bradycardia and extrasystoles were seen as well as evidence of decompensation and digestive symptoms.

The prognosis depends on the amount of cardiac damage and danger of recurrence. Seven of the patients died. The treatment consists in absolute rest in bed, morphine and quinidine. About two weeks after the attack the author gives a course of euphyllin intravenously. Digitalis is only given in small doses in cases of decompensation. If angina and hyperesthesia persist after the acute stage, the author prescribes Zülger's heart hormone and roentgen therapy.

Wassermann (page 449) contributes a small paper on the origin of heart failure psychoses. If these occur during the course of decompensation, they are to be ascribed to left ventricular insufficiency, part of which forms the cerebral anemia with Cheyne-Stokes breathing. Therefore in case of psychical symptoms in the course of heart failure the breathing should be closely watched. Separately from these he considers the psychoses which accompany the end of decompensation (terminal or agonal psychoses); these have a very bad prognosis.

The psychoses may precede the clinical decompensations in the form of slight nocturnal delirium, and they may last until the end. They belong to the category of ''fear'' psychoses and are of central origin, probably due to insufficient circulation resulting in lack of oxygen. This is explained by both their nocturnal exacerbation (sleep anoxemia) and their prevalence in cases of aortic insufficiency. The prognosis is intimately connected with that of the cardiac condition; where Cheyne-Stokes breathing occurs, oxygen therapy is of great value.

Alfred Weit (page 457) reports two cases of cardiac lesions without disturbance of function; one of a man with a bullet in his heart. The lesion presumably dates from the war, but he had no idea of its presence; not even at the time of the injury did he have symptoms; his attention at the time was drawn to a gunshot wound of the arm. The author refers to another case where a man shot himself;

the bullet severed His-Towara's bundle and produced complete heart-block; after this it became lodged in the posterior mediastinum. It produced no other effects.

The author then reports a case of peculiar right-sided enlargement of the heart, possibly an aneurysm. The remarkable thing is that a very marked enlargement has persisted for over four years without producing symptoms.

Also Hans Dietlen (page 19) contributes a case report of peculiar cardiac enlargement where the diagnosis of mitral stenosis and tricuspid insufficiency seems far from certain; neither his nor Weil's cases are accompanied by autopsy reports, all the patients still being alive.

H. Elias and J. Goldstein (page 29) differentiate between congestive heart failure of mitral stenosis and that of mitral insufficiency; they find edema in mitral stenosis is a rare and late manifestation. When it does occur, it is much less extensive than edema of mitral insufficiency. This difference holds good for all ages. On the other hand hepatic enlargement is more frequent in mitral stenosis than in insufficiency. The same holds true regarding evidence of cerebral anemia.

Fischer and Schur (page 151) record respiratory changes in the height of the pulse; they register the pulse sphygmographically over an artery compressed proximally with a cup. During inspiration the pulse becomes smaller, during expiration larger, during the interval it retains a medium size. In adherent pericarditis it became smaller during inspiration; it was largest during the respiratory pause. The respiratory changes in size are more marked than the respiratory changes in rhythm. They explain the changes in size as being due to changes in intrathoracic pressure. Finally they propose to change the term pulsus paradoxus to "Wenckebach's pulse."

Rudolf Strisower (page 445) reports on a series of experiments on feeding to rabbits cholesterol and other substances considered in the pathogenesis of hypertension. The experiments were entirely negative.

Verhandlungen der Deutschen Gesellschaft für Kreislaufforschung. Second Meeting at Bad Neuheim, March 4 and 5, 1929.

H. Siegmund: Concerning Nonsyphilitic Aortitis.

The author calls attention to lesions of the aorta; these accompany infections, particularly ulcerative and polypous endocarditis. They may, however, occur without accompanying valve defects.

They are characterized by mesaortitis without pus formation, destruction of elastic fibers and extensive destruction and scarring of the intima. In some cases *Streptococcus* viridans may be found in the blood stream. Some of these cases macroscopically look very much like luetic mesaortitis.

The lesions originate by direct implantation of more frequently by emboli through vasa vasorum. The resulting necrosis and fibrosis may be accompanied by atherosclerosis. The author also found healed lesions in routine autopsies.

Besides in ulcerative endocarditis similar lesions were found in cases of scarlet fever and rheumatic fever.

H. Mussler: Die Gesetze des Blutdruchablaufes.

The pulse pressure is a measure of the energy given to the blood stream by the heart. When the blood pressure increases, through drugs or through exercise, the diastolic pressure decreases. This is only possible with increased blood velocity which means improved circulation. At a certain increase of pulse pressure the diastolic pressure becomes constant. This is called the critical amplitude. If the pulse pressure is still further increased, the diastolic pressure increases. This results in a rapid increase in systolic pressure, this depreciates the general circulation, as the heart has a greater "resting pressure" to overcome. This results in uneconomical working. The play between normal and critical amplitude is a measure of vascular

elasticity and of cardiac reserve; it is also dependent on obstructions to the circulation. While the normal pressure is 50 mm. Hg, the critical lies about 70 to 80. In the clinical observation of the patient, the pulse pressure readings are of great importance.

P. Iversen: Oedem-pathogenese mit Bernehrungen Über Aziticpathogenese bei Herzinsufficienz.

It is in the capillaries that the shifting of water occurs from the vascular system to the intercellular connective tissue spaces. In order to understand the nature of edema one must realize that in the capillaries there are two kinds of pressure, a hydrostatic and an osmotic which is 2-300 times greater than the former. But only the fraction due to the colloids is effective, as the capillary wall is permeable to the dustalloids, which there can exert no osmotic pressure. These two pressures act against each other, and it is upon changes in the equilibrium between them that edema depends. That is, edema occurs when the hydrostatic pressure exceeds the osmotic. This may occur through increase of hydrostatic and decrease of osmotic pressure, or through a combination of the two.

The colloid osmotic pressure depends upon the percentage of protein and on the molecular size thereof. If the molecular size is greater, the osmotic pressure is smaller. Globulin has a larger molecule than albumin.

In nephrosis both the total percentage of protein and the albumin fraction in the serum are decreased. Both tend to decrease the colloid osmotic pressure below the normal hydrostatic pressure.

In heart failure patients the stasis is the important factor, because here the hydrostatic pressure increases above the colloid osmotic pressure, which furthermore is somewhat decreased partly by hydremia and partly by decrease of serum albumin through albuminuria. Besides some small but osmotically very active molecules are exceeded into the urine, this is especially marked in long-persisting but slight albuminurias.

In order to overcome edema, it is necessary to reestablish the normal equilibrium. In heart failure the cardiac tonics are used to improve the peripheral circulation; thereby the venous system is relieved, and the hydrostatic pressure in the capillaries falls, the urine secretion increases and the albuminuria disappears and the hydremia is overcome.

In ascites the same rules hold true; the varying amounts of albumin found in the exudate depend upon the stage of resorption, the greater absorption, the higher the percentage of albumin in the remaining fluid. Complete absorption only occurs after splitting up of the protein molecules.

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Original Communications

THE IMPORTANCE OF DIFFERENCES IN THE POTENCY OF DIGITALIS IN CLINICAL PRACTICE*

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About twenty years ago Hatcher and Baily[1] compared the doses of one of the digitalis bodies as recommended by different authorities and found a variation in potency as great as 750 times between the largest and smallest dosage. When one considers, therefore, the conditions that prevailed before the advent of the biological methods of assay of digitalis, when there was no way for the physician to determine in advance whether a specimen was active or inert, to say nothing of determining relative degrees of activity, one will indeed appreciate the progress that has since been made. The following recent experience in this matter is significant. A few years ago studies on digitalis dosage were undertaken in the Adult Cardiac Clinic of Bellevue Hospital, and the plan was made to compare specimens of widely different activity. There was no difficulty in obtaining very active specimens of the crude digitalis leaf on the market, but none of low activity was readily available. It was only after the examination of a large number of specimens that one was found with a potency as low as 140 milligrams to the cat unit. From this example one may perhaps overestimate the advance that has been made, but it indicates nevertheless, that the average specimen of digitalis leaf on the market is quite active and, since the U. S. Pharmacopoeia directs a fixed activity (with a limited range) for the official digitalis, the physician is fairly certain to obtain potent digitalis if the specimen complies with the requirements of the U. S. Pharmacopoeia. This progress must be attributed in a large measure to the general application of bio-assay of the drug. The more recent literature dealing with digitalis dosage has become more intelligible because, while dosage has continued in most instances to be expressed in units of weight or measure, the potency of

*From the Third (New York University) Medical Division of Bellevue Hospital and the Department of Pharmacology of Cornell University Medical College.

the specimens is frequently stated, affording in this way some basis of comparison of the experience of different workers. The Cardiac Clinics of the New York Tuberculosis and Health Association have adopted the plan of dispensing digitalis tablets in terms of their activity (cat units) rather than weight, though the equivalent in weight is stated.

It is perhaps quite generally appreciated among physicians that the bio-assay of digitalis is an important determination but it is well known that the average physician makes little use of the data thus obtained, and an examination of the literature reveals the fact that at the present time there is a great deal of misunderstanding in regard to what use the physician should make of the results of this procedure. The need for accurate knowledge regarding the strength of digitalis was called to our attention with great force by the experience of the Committee* for the study of digitalis in pneumonia at Bellevue Hospital. In this communication† an effort is made to clarify some of the issues involved in the application of the bio-assay of digitalis to clinical practice, based upon some of the results obtained by this Committee as well as upon the studies on digitalis dosage in the Adult Cardiac Clinic, both of which will be reported in detail at another time.

Only those facts regarding the work of the Committee necessary for the present analysis will be considered in this report which involves a comparison of some of the data obtained with two preparations of digitalis used in a series of 248 patients with pneumonia.

Two commercial preparations of dried digitalis leaf were used. According to the statements on the labels, one, specimen "A," contained 100 milligrams per cat unit and the other, specimen "B," contained 65 milligrams per cat unit. These statements of potency were at first assumed to be correct and the doses were calculated and administered on that basis. Specimen "A" was dispensed in the form of compressed tablets only; Specimen "B," partly in tablets and partly in capsules that are supplied by the manufacturer.

Table I shows the general plan of dosage employed in the study. At first patients were divided into three weight groups of 125, 150, and 175 pounds respectively. The full dose for each group was calculated on the basis of approximately 0.15 cat unit per pound of body weight, so that the patients in the three groups were to receive a total dose of 18, 22, and 26 cat units respectively. The actual quantities of the drug by weight as seen in the table were smaller for the stronger than for the weaker preparation. The total quantity for each patient was divided into fractions of 30, 30, 15, 15, and 10 per cent respectively

*The Committee was composed of representatives of the First (Columbia University) Medical Division, the Second (Cornell University) Medical Division and the Third (New York University) Medical Division of Bellevue Hospital.

†A preliminary discussion of this subject has been published in the J. A. M. A. 94: 626, 1930.

and given at six hour intervals so that the full dose was administered in about twenty-four hours. If no toxic symptoms appeared a daily maintenance dose of two cat units was then continued. In the course of the work it became necessary for reasons that we shall presently see to reduce the size of the full dose (the smaller dose method of Table I)

TABLE I

SHOWING TOTAL DOSES OF DIGITALIS FOR PATIENTS OF DIFFERENT WEIGHT GROUPS CALCULATED ON BASIS OF POTENCY STATED BY THE MANUFACTURER

METHOD AND PREPARATION	TOTAL DOSES		
	AVERAGE 125 LB.	AVERAGE 150 LB.	AVERAGE 175 LB.
Larger dose method	(18 C. U.)	(22 C. U.)	(26 C. U.)
Specimen "A"	1.80 Gm. (27 gr.)	2.20 Gm. (33 gr.)	2.60 Gm. (39 gr.)
Specimen "B"	1.20 Gm. (18 gr.)	1.47 Gm. (22 gr.)	1.73 Gm. (26 gr.)
	BELOW 150 LB.	ABOVE 150 LB.	
Smaller dose method	(10 C. U.)	(12.5 C. U.)	
Specimen "A"	1.00 Gm. (15 gr.)	1.25 Gm. (18.75 gr.)	
Specimen "B"	0.66 Gm. (10 gr.)	0.83 Gm. (12.5 gr.)	

(C. U.) Cat Units.

TABLE II

SHOWING TOTAL DOSES OF DIGITALIS ACTUALLY RECEIVED BY PATIENTS IN DIFFERENT WEIGHT GROUPS ON THE BASIS OF THE TRUE POTENCY

METHOD AND PREPARATION	TOTAL DOSES		
	AVERAGE 125 LB.	AVERAGE 150 LB.	AVERAGE 175 LB.
Larger dose method	18 C. U.	22 C. U.	26 C. U.
Specimen "A"	(1.8 Gm. or 27 gr.)	(2.2 Gm. or 33 gr.)	(2.6 Gm. or 39 gr.)
	36 C. U.	44 C. U.	52 C. U.
Specimen "B"	(2.4 Gm. or 36 gr.)	(2.94 Gm. or 44 gr.)	(3.46 Gm. or 52 gr.)
	BELOW 150 LB.	ABOVE 150 LB.	
Smaller dose method	10 C. U.	12.5 C. U.	
Specimen "A"	(1.0 Gm. or 15 gr.)	(1.25 Gm. or 18.75 gr.)	
	20 C. U.	25 C. U.	
Specimen "B"	(1.32 Gm. or 20 gr.)	(1.66 Gm. or 25 gr.)	

and only two weight groups were then considered, those under 150 pounds receiving 10 cat units and those above 150 pounds receiving 12.5 cat units. These doses were administered in fractions of 50, 25, and 25 per cent of the total respectively, twelve to eighteen hours elapsing between the first and second dose, and six to eight hours between the second and third dose. A daily maintenance dose of 2 cat units was then administered as in the first method.

Table III shows the incidence of toxic symptoms with the two preparations of digitalis. By the larger dose method, vomiting occurred in only 3.7 per cent of the patients receiving specimen "A" as against 38.4 per cent of those receiving specimen "B". Similarly only 4.9 per cent of the former developed the higher grades of heart-block as against 14.9 per cent for the latter. The total number of patients in

the group receiving digitalis by the smaller dose method is too small to draw conclusions from it by itself; nevertheless, it bears out the results obtained with the larger dose method, namely, a relatively greater incidence of toxic phenomena with specimen "B".

TABLE III

SHOWING INCIDENCE OF TOXIC PHENOMENA WITH THE TWO PREPARATIONS OF DIGITALIS

METHOD	SPECIMEN	TOTAL NUMBER PATIENTS	NO. OF PATIENTS AND INCIDENCE OF TOXIC EFFECTS		
			VOMITING	FIRST STAGE BLOCK ONLY	SECOND, THIRD, FOURTH STAGES BLOCK
Larger dose	"A"	82	3 (3.7%)	23 (28.0%)	4 (4.9%)
Larger dose	"B"	125	48 (38.4%)	33 (26.4%)	18 (14.4%)
Smaller dose	"A"	11	0 (0.0%)	1 (9.1%)	0 (0.0%)
Smaller dose	"B"	30	6 (20.0%)	8 (26.7%)	3 (10.0%)

TABLE IV

SHOWING THE NUMBER OF DOSES ADMINISTERED BEFORE VOMITING WITH THE TWO SPECIMENS OF DIGITALIS

SPECIMEN	"A"		"B"	
NUMBER OF DOSES OF DIGITALIS	NUMBER OF PATIENTS WITH LARGE DOSE METHOD	NUMBER OF PATIENTS WITH SMALL DOSE METHOD	NUMBER OF PATIENTS WITH LARGE DOSE METHOD	NUMBER OF PATIENTS WITH SMALL DOSE METHOD
1	0	0	0	0
2	2	0	17	0
3	0	0	5	0
4	0	0	1	2
5	0	0	20	0
6	0	0	2	0
7	0	0	1	2
8	0	0	1	1
9	0	0	0	0
10	0	0	0	1
11	1	0	1	0

There can be no question that the greater incidence of toxic phenomena with specimen "B" was due to the systemic action of the drug. When vomiting appeared the drug was discontinued, but, as seen in Table IV, at least two-thirds of the total dose had been administered before vomiting occurred. The types of patients in the groups receiving the different specimens of digitalis were fairly comparable, about forty per cent of each being represented by the Pneumococcus Types II and III. The incidence of symptoms similar to the toxic phenomena in large groups of untreated controls was practically negligible.* The relatively greater systemic toxic action of this specimen of digitalis was further confirmed by the relatively greater incidence of the higher grades of heart-block.

*These matters will be discussed in detail in subsequent reports of the Committee.

DISCUSSION

Although the essentials of the present discussion refer also to other methods of digitalis assay, we shall speak in terms of the cat method in order to be more concrete, and because more experience has been

TABLE V

SHOWING INCIDENCE OF VOMITING IN DIFFERENT WEIGHT GROUPS WITH SPECIMEN "B"

WEIGHT GROUPS	LARGER DOSE METHOD		
	AVERAGE 125 LB.	AVERAGE 150 LB.	AVERAGE 175 LB.
Total doses*	36 C.U.	44 C.U.	52 C.U.
Total no. patients	48	67	10
Number vomited	21	21	6
Incidence of vomiting	43.8%	31.3%	60%
WEIGHT GROUPS	SMALLER DOSE METHOD		
	BELOW 150 LB.	ABOVE 150 LB.	
Total doses*	20 C.U.	25 C.U.	
Total no. patients	20	10	
Number vomited	4	2	
Incidence of vomiting	20%	20%	

*On basis of corrected potency.

recorded regarding the application of cat units to clinical use of the drug than of any other biological units. Two distinct principles are involved in the bio-assay of digitalis by the cat method. First, the average normal cat requires a fairly fixed quantity of a given specimen of digitalis per unit of body weight to cause death. Variations are always present, and occasionally very marked, but with a uniform technique satisfactory averages can be obtained. Second, differences in activity of different digitalis preparations can be detected by this method. Both principles have been applied to man, which in turn has given rise to the question as to whether they are true for man and to what extent they are practical.

Eggleston[2] found that when he digitalized a group of patients with a number of digitalis preparations of different cat unit strengths, the doses proved to be most uniform when expressed in terms of cat units per pound of body weight. He did not state that this method would yield the exact dose for any single individual. He showed, as many others have also seen, that there are marked variations in the doses for different patients, but that the range of variation was wider when the doses were expressed as total quantity per patient than when expressed as cat unit per pound of body weight. In a recent study Martin[3] confirmed the relationship between total dosage, the body weight of patients, and the biological activity of different specimens of digitalis. Scores of workers have availed themselves of that technique and have thereby popularized the large dose method of administering digitalis. It is necessary to bear in mind that both principles are here involved; (1) that body weight is a factor in digitalis dosage, and

(2) if one specimen is found to be more active than another in cats, it will also be found more active in man.

Some authors have questioned the validity of these conclusions and some, their practical value. H. J. Stewart[4] recently made the following statements: "Experience has shown that the biologic assay of the drug (digitalis) by the cat or by the frog method does not parallel the therapeutic effect in patients. The amount, however, of any preparation that is required to give this effect is approximately the same regardless of the age and the weight of the patient." There are no potent drugs in the materia medica that one would venture to give to patients of five or six years of age, or to those weighing forty or fifty pounds, in the same doses required for full effects in adults weighing 150 to 175 pounds. When digitalis, like any other drug, enters the circulation, it is distributed throughout the entire body and is taken up by many tissues, only a fraction of the total reaching the heart. Hence if one patient weighs twice as much as another, the same dose will result in a smaller allotment for the heart.

The principle that body weight and dosage are related simply expresses the idea that a very small man will require less digitalis than a very large man to produce a given effect, other conditions being the same. In actual practice, these other conditions are usually not found to be the same. This merely places a limitation on the value of the weight factor, since there are many variables to be dealt with in the treatment of heart disease, among which body weight is only one. For example, the average ambulatory cardiac patient usually does not require the same degree of digitalization found necessary for the average patient in acute congestive heart failure, and even though these two patients may be of the same weight, a difference in their degree of failure may make it necessary to give one much larger doses of digitalis than the other.[5] The nearer the weights of patients approach each other between such extremes as mentioned above, the less apparent does the weight factor become. The counterplay of the many variable factors makes it a matter of some difficulty to estimate the rôle of any one, and under such conditions a few studies confirming a sound principle are probably more nearly correct than a number that fail to do so. An interesting indication of the body weight factor is seen in Table V, in which the patients of the pneumonia series were distributed into groups according to weight in order to determine the incidence of vomiting in each. The number of patients in the 175 pound group is too small to be considered. Of the patients in the 150 and 125 pound groups, the former or heavier, received twenty-two per cent more digitalis than the latter or lighter group. If no relationship between body weight and dosage exists among adults, the group which received more digitalis would have shown a greater incidence of vomiting. Our justification for the assumption that the effect of a

twenty-two per cent greater dose could be detected is the fact that the patients in the lighter group were already receiving a rather toxic dose, namely, one after which nearly one-half of the patients vomited. The results do not show a greater incidence of vomiting in the heavier group, favoring, therefore, the probability that the body weight was a factor in the dosage. There can be little question that under suitable conditions body weight can be shown to be a factor in digitalis dosage as in that of any other potent drug. If one attempts to use the body weight factor to determine differences in the amount of digitalis required by a patient of 130 pounds with arteriosclerotic heart disease showing mild signs of heart failure and that by a young patient of 150 pounds with rheumatic heart disease showing acute congestive heart failure, there can be little surprise if one detects no relationship whatsoever between dosage and body weight. The value of using the factor of body weight in estimating dosage has been obscured by those who have attempted to employ it as a fixed rule of thumb, as a substitute for, rather than as a helpful guide to, the principle of dosage which is, in the last analysis, to give enough to produce full therapeutic effects and not so much as to produce toxic effects.

The second principle relating to biological activity of digitalis is more important from the practical standpoint. Stewart stated that the biological assay of digitalis does not parallel the therapeutic effect in patients, and that of a commercial specimen, digitan, which he has used for years, one gram given by mouth within twenty-four hours usually produces satisfactory full digitalization. Let us now ask how his experience can be translated into terms intelligible to those who do not use digitan. Is his experience different from that of scores of other workers who have found that it requires about one and one-half to two grams of active digitalis to produce full effects, or is it the same, the differences in the quantities stated being due merely to differences in activity of the preparations used? There is no way of knowing from his report, because digitan is assayed by the frog method of Gottlieb, a method not official in the U.S. Pharmacopoeia and not in common use in this country, and no satisfactory data are available for translating these into cat units or standard frog units of the U.S. Pharmacopoeia. Furthermore, there is no assurance that digitan is of constant activity because the method of Gottlieb does not require the standardization of frogs, the susceptibility of which is known to vary considerably. As it stands, therefore, the dosage of digitalis given by Stewart differs from that of many other observers, but it is not possible to know whether or not a new fact has been uncovered, because in a sense, the different authors do not speak the same language.

From all facts at present available, it would be sound to assume that if one specimen of digitalis is twice as active as another when it is

brought into contact with the cat's heart at a given rate, the same relative activity between the two would be present in man (though not necessarily the same absolute activity) under similar conditions. But since the drug is usually given by mouth in man, the factors of absorption and elimination complicate the determinations of the relative activity of any two preparations. Obviously when two specimens of digitalis have the same activity, but differ in rate of absorption and elimination, their dosage may be different. This simply places a theoretical limitation on the value of bio-assay by the cat method, and makes it necessary to bear in mind that if one specimen is twice as active as another by intravenous injection into the cat, it may not necessarily be twice as active by oral administration in man. But in actual practice, barring the occasional specimen of digitalis that is poorly absorbed, one finds that preparations with significant differences in biological activity by the cat method reveal these differences when used in man, if suitable conditions are present to detect them. Patients can often tolerate much larger doses of digitalis than are necessary to maintain a condition of optimum improvement.[5] It is in this range between the minimum necessary dose and the maximum tolerated dose that moderate differences in biological activity of digitalis escape notice in clinical practice. This again does not vitiate the practical value of biological assay. A more vigorous method of digitalis dosage, on the contrary, shows the indispensability of an accurate knowledge of the relative potency of digitalis preparations, as was illustrated by the experience of the Pneumonia Committee. As already stated, two well-known commercial specimens of digitalis leaf were employed, one about fifty per cent more active than the other, according to the labels of the manufacturers The toxic symptom, vomiting, occurred in more than ten times as many patients with that specimen which was given in smaller doses in terms of grains (specimen "B") although a uniform technique was employed and comparable doses of the two preparations were given in terms of their supposed potency. This, on the surface, seemed to support Stewart's statement that biological assay does not parallel the therapeutic effect in patients. The two specimens were then tested by the cat method in the Department of Pharmacology of Cornell University Medical College. The results showed that the tincture of specimen "A" had the potency stated on the label, namely, one c.c. per cat unit, while the tincture of specimen "B" was found to have a potency of about 0.4 c.c. instead of 0.65 c.c. per cat unit. The latter tincture was tested independently by the cat method in the Department of Pharmacology of the University of Michigan and the results agreed with those obtained at Cornell, namely, that the tincture of specimen "B" was about sixty per cent more active than was stated by the manufacturer. The tablets of specimen "B" were then examined biologically, and this resulted in the discovery that each tab-

let did not represent one cat unit as stated on the label, but two cat units. Hence, the tablets of specimen "B" were 100 per cent stronger than the statement by the manufacturer indicated. Since the tablet contained some inert matter it was impossible to state whether the greater strength of each tablet was due to a greater potency of the digitalis leaf itself, or whether each tablet simply contained two grains of digitalis instead of one.

With these facts in hand the total doses of specimen "B" that were received by the pneumonia patients were recalculated. These are shown in Table II. While it was at first believed (see Table I) that the patients were receiving comparable doses of the two preparations, the results in Table II show that on the basis of the true potency, those treated with specimen "B" actually received twice as much digitalis as those with specimen "A", and this accounted for the high incidence of toxicity with the former preparation. A more suitable example could hardly be found that shows the close parallelism existing between the cat method of bio-assay of digitalis and the effects in man. An erroneous statement regarding the cat unit potency was promptly detected in the form of toxic symptoms in patients when comparatively large doses of digitalis were used. If very small doses had been used, it is indeed probable that the misstatement of the manufacturer regarding the activity of the drug would have escaped detection.

This brings us to a related matter about which a better understanding is necessary. Levy and Mackie[6] in a recent paper advocated the use of "standardized digitalis" and stated the average full dose to be about 1.5 grams under certain conditions. The word "standardized", however, does not have a fixed meaning, the U.S. Pharmacopoeia having one standard and the various manufacturers having their own standards. The importance of these differences in standards may be seen from the following example. Each of two well-known commercial specimens of digitalis are referred to on the labels as "standardized", yet one is stated to have a cat unit strength of 100 milligrams, and the other a cat unit strength of 65 milligrams. The question at once arises to which, if any, of these preparations does the statement of Levy and Mackie refer, in which they say that 1.5 grams is the average full dose of "standardized digitalis", since one of these so-called "standardized" preparations may contain about one and one-half times the activity of the other in the 1.5 gram dose. Another commercial specimen of digitalis which has proved to be quite active merely bears the label "physiologically tested" as if the results of that test were of interest only to the manufacturer. The condition is somewhat analogous to a physician sending a specimen of blood for a urea determination and finding that the only report available is that the determination has been made. Physiological testing is essentially a quantitative determination, not so much to ascertain whether a given preparation has digitalis action as to determine by how

much one specimen is stronger than another. Compliance with the requirements of the U.S. Pharmacopoeia does not in itself insure sufficient uniformity in strength for accurate clinical studies because two specimens of digitalis may meet the official requirements and yet one may be as much as thirty per cent more active than another by the frog method. Again it is necessary to emphasize what we have already stated, that under many conditions these differences in the potency of digitalis may escape detection in practice, but where large doses are necessary a knowledge of these differences will avoid a great deal of unsatisfactory use of the drug in the nature of excessive or insufficient digitalization.

There are many points of similarity between the problem of the dosage of digitalis and that of insulin. Both drugs vary in activity and are assayed biologically. No one would doubt that it is irrational to speak of insulin dosage in terms of c.c. without naming the standard, because one c.c. of insulin may contain 20, 40, or 80 units. Nevertheless, it is common practice to refer to the dosage of the tincture of digitalis in terms of c.c. without stating the potency, though it is equally irrational because a c.c. of one specimen of the tincture may represent one cat unit, while that of another specimen may represent two or more cat units.

Finally, it is necessary to call attention to the question of the bearing of the biological strength of digitalis upon the relative merits of different preparations. Obviously, in order to be of therapeutic value, digitalis must be active. But the views commonly held that one digitalis preparation is better than another because one is 25 or 50 per cent, or even 100 per cent, more active than another, does not display a sufficient sense of relative values. There are preparations of digitalis on the market of which the sole claim to superiority is a fifty per cent greater activity as determined by bio-assay. The only possible advantage of a more active specimen from a therapeutic standpoint would be the diminished bulk of the individual doses. If the biological assay shows one preparation to be weaker than another within reasonable limits (differences of as high as 100 per cent are not commonly seen), it is of course necessary to give a larger quantity of the weaker preparation. What possible difference does it make, however, whether a patient receives a daily dose of two grains of the stronger or so-called "good" preparation instead of a dose of three or four grains of the weaker or so-called "poor" preparation? Since digitalis is a potent drug, the dosage of which is measured in quantities of grains, and not ounces or pounds, bulk can rarely be a matter of any importance, and the fact that a few additional grains may be necessary in the case of the weaker preparation affords no reasonable objection to it. The general interest in the question of "stronger" and "weaker" preparations has only served to obscure the significance of the fact that it is a matter of no

importance whether one preparation is stronger or weaker than another (within reasonable limits), provided one knows the exact potency of each.

SUMMARY

1. This communication deals with an analysis of the factors involved in the application of the bio-assay of digitalis by the cat method to clinical practice.

2. Evidence is presented showing that body weight is a factor in digitalis dosage and that it is essential to take into account differences in potency of digitalis as determined by bio-assay.

3. It is pointed out that when small doses of digitalis are used, the value of both factors (body weight and differences in potency) may escape detection.

4. An analysis is made of the experience of the Committee for the study of digitalis in pneumonia at Bellevue Hospital with a well-known commercial preparation of digitalis, the potency of which was later proven to have been incorrectly labelled by the manufacturer. This analysis shows in the first place, that a specimen of digitalis which was found to be about twice as active as anticipated for man proved to be also twice as active by the cat method of assay; and secondly, it shows the dangers arising from the use of digitalis, especially in large doses, without knowing the exact potency.

5. Evidence is presented showing the confusion which arises from the use of the term "standardized digitalis" without stating the exact potency because of the different standards used by the various manufacturers.

6. The relative merits of so-called "stronger" and "weaker" preparations of digitalis are discussed.

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TWO CASES OF COMPLETE OCCLUSION OF BOTH CORONARY ORIFICES*

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IT IS now generally conceded that of all the smaller vessels of the body whose function is necessary to the continuation of life none are more essential than the coronary arteries. The sudden dramatic termination of life which so frequently results from the occlusion of a branch of a coronary artery furnishes ample support for this thesis. Death from coronary obstruction may be and frequently is the most sudden form of death known. A man may literally drop dead. So characteristic is the manner of death that a usually successful snap diagnosis may be made from that evidence alone. Deaths from cyanide poisoning and those occurring in certain cases of hypertensive heart disease with edema of the brain, practically alone rival coronary occlusion in the rapidity with which death may be produced. (Sudden deaths from aortic insufficiency, in which the coronary orifices are not occluded, are due to interference with the coronary blood supply, in our opinion.)

On the other hand, it is well known that extensive lesions of the coronary arteries may exist for long periods of time without manifest debilitating effect and even without any clinical signs or symptoms whatsoever. There are many cases on record where the fatal occlusion of the artery led to the first suspicion of the presence of coronary disease.

As medical examiner of Suffolk County, one of us (T. L.) is called upon to investigate deaths of human beings, supposedly due to violence. This term has been interpreted to include deaths in which the causation is not apparent or adequate. Under this provision there come under the jurisdiction of the medical examiner a number of cases in which investigation discloses that death was due to natural causes or disease. As is to be expected this group embraces a considerable percentage of sudden deaths in which the cardiac circulation is at fault.

Among the cases of this character seen in recent years are the following two, in which there was essentially complete obliteration of both coronary orifices.

*From the Medical Examiner Service of Suffolk County and the Boston City Hospital.

CASE REPORTS

CASE 1.—J. B., Swedish male, white, thirty-five years old, had been in America for eighteen years. His principal occupation had been that of a sailor. His uncle who brought him to this country complained that he never stuck to any job for a long time. During intervals between sailings he had worked off and on for a local awning company as an extra man. The work of this company is seasonal, awnings being put up in the spring and taken down in the fall. He had been out of work much of the winter of 1925-1926, not because of illness, but because of difficulty in getting work. He worked for the awning company from April 30 to August 5, 1926, and was then laid off with other extra men. He was employed again October 5 and worked until November 5 when extra work stopped for the year. During this latter period he worked five or six days per week. He was seen by his uncle two weeks before his death, at which time he had a cold and looked badly. He told his uncle he had been carrying heavy awnings and awning rods in the rain and had caught cold. His uncle stated that he had a ''raving'' appetite and ate too much. As a result he had ''stomach trouble—indigestion.'' He had suffered from headaches for years. He did not drink but smoked many cigarettes. He had not been treated by a doctor since he came to this country.

He roomed in a lodging house and was last seen alive November 10, 1926, at 7 A.M. He was found dead in bed by his landlady on November 11 at 1:30 P.M. When found, he was clothed, though in bed, in a wool sweater over a cotton union suit and with a khaki wool scarf wound about his waist. From the appearance of the body it was evident that death had occurred probably twenty-four hours or more before its discovery.

At the post-mortem examination the heart cavities contained gas and frothy fluid blood which was hemolized. Smears furnished abundant gram-positive bacilli, with B. welchii morphology. Heart and aorta showed some staining of surfaces with blood coloring matter. Each pleural cavity contained a fluid stained with blood coloring matter, the right 225 c.c. the left 150 c.c. The long delay in the discovery of the body, which was covered with excess clothing, had evidently favored the post-mortem incubation of B. welchii.

The pathological findings of interest were confined to the heart and aorta. Otherwise nothing remarkable was found.

The pericardium was smooth and lustrous, containing 5 c.c. of blood-tinged fluid.

Heart weighed 328 grams. The heart muscle was flabby, gray red. Wall of left ventricle measured 1.4 cm.; wall of right ventricle measured 0.5 cm.; mitral valve measured 8.6 cm.; aortic valve measured 7 cm.; 5 cm. above ring, aorta measured 8.5 cm.; pulmonary valve measured 7.8 cm.; tricuspid valve measured 10.3 cm.; depth of left ventricle measured 7.3 cm.

On section the heart muscle was homogeneous, disclosing no evidence of fibrous tissue.

The ascending arch of the aorta showed a continuous series of irregular masses of raised, nodular, translucent and opaque, gray white tissue encircling the vessel above the ring and extending into the sinuses of Valsalva. This girdle (girdle of Venus?) measured 1.8 cm. in breadth at its narrowest point above the right coronary sinus and extended for 6 cm. above the ring over the left coronary sinus along the region of contact of the aorta with the pulmonary artery. The process of scarring and thickening of the aortic wall extended into the depths of the right coronary sinus to its lowest limit. In the left and noncoronary sinuses the wall was thickened only in the upper part of each sinus, the wall of the noncoronary sinus showing thinning in its lower portion, measuring only 0.1 cm. in thickness.

The site of the orifice of the right coronary artery was occupied by nodular scar tissue without suggestion of the location of the original orifice. The site of

Fig. 1.—Case 1. Drawing of the heart and ascending arch of aorta. Below are drawings of the cross-sections of the left coronary and right coronary respectively, as they are seen from the rear within the aortic wall (enlarged 3 diameters).

the orifice of the left coronary artery was indicated by a shallow dimple. Serial sections through the tissue behind the aortic wall disclosed grossly complete obliteration of the proximal portions of both coronary arteries by a relatively translucent gray tissue. This obliteration extended just through the adventitia of the aorta in either case and stopped abruptly. The coronary arteries beyond this obstruction showed a wall of apparently less than normal thickness. The vessels were of small caliber and were filled with blood.

There was some dilatation of the left ventricle due probably in part to the frothy blood and gas found within the cavity post-mortem. Otherwise, apart from slight thickening of the free edges of the aortic cusps, particularly about the corpora Arantii, the valves and cavities were normal.

The aorta showed in transverse and descending arches few small and larger, slightly raised, gray white nodules. The thoracic and abdominal aorta was thin, smooth and elastic.

The lungs showed a moderate edema.

Microscopical examination of the coronary arteries was carried out by shaving pieces from the back of the aorta. These pieces were then imbedded and sectioned. The actual point of most complete obliteration in each artery was in relation to the intima of the aorta.

Right Coronary Artery.—The lumen of the vessel was obliterated, save for a very small eccentric opening, by young, relatively cellular connective tissue from the subendothelial layer. Through one segment of the media of the coronary artery a collection of vasa vasorum, evidently arising from the adventitia of the aorta, were thrust through the coronary media to enter the young intimal tissue. The media was otherwise not remarkable. In the adventitia and surrounding tissue there was edema with large focal collections of lymphoid and plasma cells, some of which were perivascular. Stains for study of the elastica were unsatisfactory because of poor preservation.

Left Coronary.—Microscopical examination showed obliteration of lumen save for a small opening, eccentric, but less markedly so than in the right coronary. The original lumen was largely filled with old, relatively acellular hyaline and vacuolated connective tissue, particularly about the region of the small vascular opening. Along the wall at either end of the oval contour of vessel, there were considerable collections of round cells in younger connective tissue, with multiple canaliculi. The muscle wall showed marked thinning in one segment, and surrounding tissue contained large collections of round cells.

The heart muscle was normal, without fragmentation or segmentation. There was no increase of connective tissue and no round cell infiltration. The vessels were normal. Sections stained with scharlach r showed no fatty metamorphosis of muscle.

CASE 2.—L. F. J., a single colored woman, twenty-six years of age, lived in the rear of a small store owned by her lover. She went out daily as a dressmaker to within a few days of her death. She was said to have had acute indigestion for several days before her death. She was found dead at 1:20 A.M., January 21, 1926, having been last seen alive at 10 P.M., January 20. Investigation later revealed that she had been treated by a local doctor on two occasions in the month preceding her death. She complained to him that she was tired and short of breath. He found a systolic blood pressure of 180-190, diastolic 90-100, with a systolic murmur. The area of cardiac dullness was increased. He made a diagnosis of hypertension.

The woman's lover reported that she had been perfectly well up to two months before her death. She collapsed in the street and since that time had had five similar attacks of "going limp." All but the first attack occurred at night

under sexual excitement. He applied hot fomentations over the breast, and with rubbing she "came to" in a few minutes.

The body was that of a slender, café au lait negress, 5 feet 1½ inches, well developed and nourished; brown eyes, pupils equal, 0.5 cm. The body was fully clothed. There were vomitus and dried froth over neck and left shoulder. Breasts were small and showed large pigmented areola. No contents could be expressed. Fingers were not clubbed.

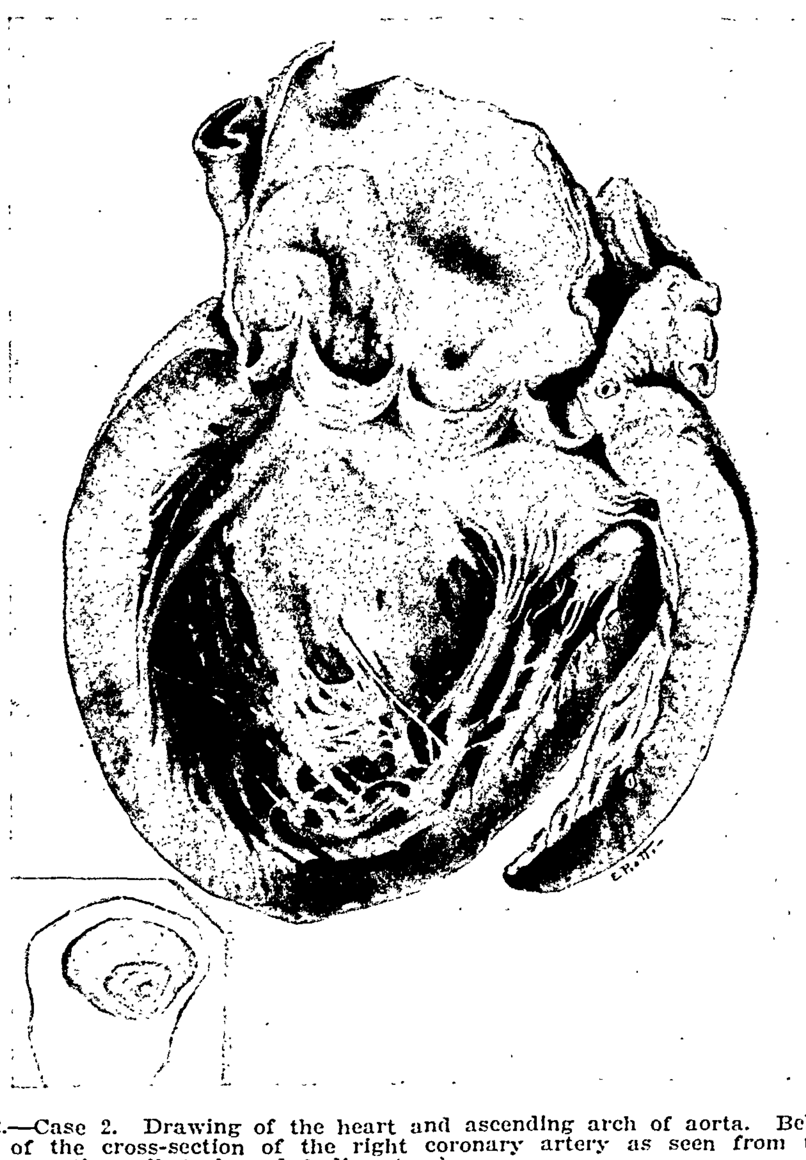

Fig. 2.—Case 2. Drawing of the heart and ascending arch of aorta. Below is a drawing of the cross-section of the right coronary artery as seen from the rear within the aortic wall (enlarged 3 diameters).

As in Case 1 the significant post-mortem findings, apart from an old repaired salpingitis, perisalpingitis and periovaritis, and the occurrence of uterine myomata, were limited to the heart and aorta.

The pericardium was smooth; contained 5 c.c. of a clear serous fluid.

The vessels of the neck and the cavities of the right heart were widely distended with fluid blood and a small amount of lax mixed clot.

The heart weighed 285 grams. The heart muscle was light red, firm, homogeneous.

Heart measurements:

Wall of left ventricle measured 1.2 cm.; wall of right ventricle measured 0.45 cm.; mitral valve measured 8.4 cm.; aortic valve measured 7 cm.; pulmonary valve measured 6.4 cm.; tricuspid valve measured 10.1 cm.; depth of left ventricle measured 7.2 cm.

Valves and cavities were normal.

The arch of the aorta showed a crescentic zone of slightly raised, nodular thickening, incomplete over the noncoronary sinus, extending 3.5 cm. above the ring over the left and the right coronary sinuses. The site of the orifice of the right coronary artery was occupied by smooth scar tissue. In opening the heart the enterotome cut through the left coronary artery near the orifice. Viewed from behind the left coronary was of normal caliber, which narrowed sharply to closure. A slight dimple in the surface of the aorta marked the site of the orifice. The ascending arch apart from these lesions, and a few small pinhead yellow foci were thin and smooth. The aortic cusps showed no thickening or other changes. The aorta below the arch was thin, smooth and elastic.

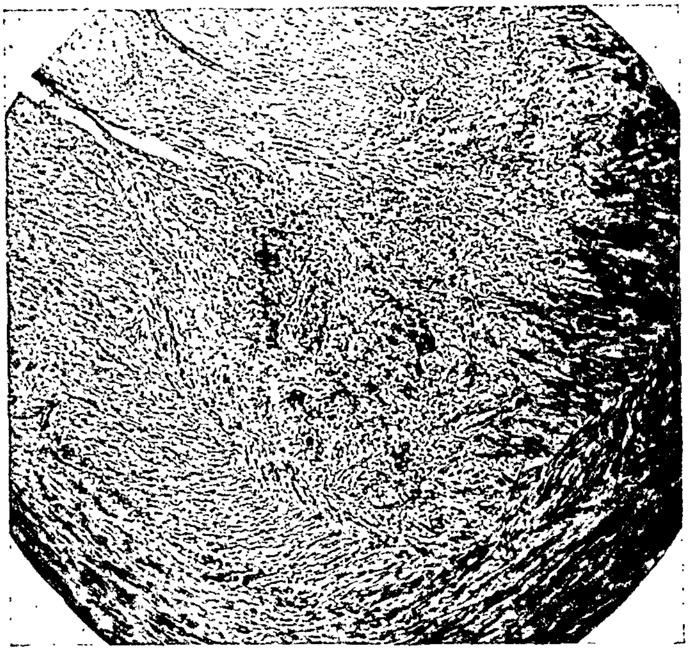

Fig. 3.—Photomicrograph of portion of occluded right coronary artery, Case 2, to show vasa vasorum passing through wall (enlarged 80 times).

Microscopic examination of the right coronary artery in the region of obstruction showed the lumen of the vessel obliterated. Near one end the occlusion was due to an older, more hyaline, and relatively acellular connective tissue. Throughout this tissue, however, were distributed small collections of lymphoid cells, for the most part in rows, with larger collections near the junction of the intima and media. Toward the other end occurred a younger, more cellular, less hyaline, connective tissue containing vessels and exhibiting dense collections of round cells, notably about the vessels. The infiltrating cells were largely lymphoid and plasma cells, with some histiocytes. The vessels were numerous and, except in the vessels of small caliber along the junction with media at one point, bore no resemblance to the irregular clefts converted into vessels which are seen in the canalization of a thrombus. The invading arteries were readily identifiable as such. The muscle coat of the occluded coronary showed in places collections of round cells, particularly about arteries penetrating this layer, and hyaline changes with thickening and

thinning of the muscle coat were apparent along one segment of the vessel wall. The surrounding fatty and connective tissue harbored massive collections of infiltrating cells about blood vessels.

The left coronary artery showed on microscopical examination an abrupt narrowing as it passed through the aortic wall. The lumen of the vessel was distorted and compressed by a high grade edema of the subintimal layer of the intima, associated with the occurrence of fibroblasts, histocytes, and lymphoid and plasma cells. The infiltration with small round cells was more diffuse and more marked in this lesion than in the three other coronaries thus far considered.

After long fixation in Kaiserling with loss of fluid, thinning and retraction of the lesion in the aortic wall, a line representing the lumen of this vessel could be grossly followed through the aortic wall.

DISCUSSION OF THE PATHOLOGY OF THE LESIONS

In most of the forms of obliterative endarteritis of vessels of the size of the coronaries the complete occlusion of the lumen has depended in part upon thrombus formation, early or late, to be followed by organization of the thrombus.

Klotz[1] says that rarely if ever does obliteration of a vessel take place as a result of an internal proliferation simply. He found that the complete occlusion was due to thrombosis. Gurd and Wade[2] describe obliterative lesions in small vessels (less than 1 mm. in diameter) due wholly to proliferation of the intima.

In the physiological obliteration of the ductus arteriosus and the upper portions of the hypogastric arteries, following birth, contraction of the wall, followed by subendothelial growth of the intima rapidly convert the vessels into fibrous cords with minimal thrombosis. Accompanying and following the involution of the uterus and ovaries, a productive endarteritis may arise. But in the latter group thrombosis may be a factor in leading to occlusion of the lumen. In thromboangiitis obliterans and in syphilitic processes in the cerebral or peripheral vessels thrombosis is the standard means of closing the lumen. In the lesions with which our paper deals thrombosis plays no part. The closure of three of the four vessels is dependent upon a progressive increase of the subendothelial layer of the coronary intima which narrows the lumen to such a degree that ultimately it becomes so small that it cannot be differentiated from the vasa vasorum which supply the organizing tissue. These vasa vasorum, supplying the aorta, penetrate through the muscle coat of the coronary arteries and are responsible for the character of the process, which is limited sharply to that portion of the coronary arteries which lies within the aortic wall. This form of obliterative endarteritis is remarkable in that the organizing agencies which obliterate the canal are not dependent upon the powers of the affected vessels but are derived from more potent forces from without the vessel to be occluded. These conditions can practically only obtain in relation to the branches of the aorta as they pass through the aortic wall. The process preserves

the integrity of the endothelium lining the coronary lumen so that thrombosis does not occur. There are no degenerative changes other than hyaline in the subendothelial layer, so that the endothelium is well supported throughout the progress of the disease. There is little distortion and no flattening of the lumen, which is progressively narrowed and modified to accommodate it to new conditions, until ultimately it has shrunk to the dimensions of one of the invading vasa vasorum, from which it cannot be differentiated.

The Degree of Occlusion.—The heart in Case 1 showed grossly complete obliteration of both coronary arteries not only at the orifices but throughout the thickness of the aortic wall. This is also true of the right coronary in Case 2. In the left coronary of this case the occlusion was dependent in considerable part upon edema of the thickened intima of the aorta. Injection of fluid into the coronary arteries behind the aorta in each of these four vessels, after the hearts had been fixed in Kaiserling, resulted in the delivery of no fluid onto the aortic surface. The occlusion was apparently complete. From the nature of the obliterative process, however, which preserves the original lumen, it seemed probable that some fluid should make its way through the small lumen which persisted. An opportunity to test this presented itself in the fresh heart of a third case in which the right coronary orifice alone was obliterated. In this case the right coronary artery was tied 2 cm. from the aorta, and saline solution was injected with some force from behind. Fluid escaped onto the surface of the aorta in drops which formed and broke as though the delivery were from a small vessel. The opening through which the fluid escaped onto the aortic surface was too small to be seen.

The question of the degree of occlusion is from the practical standpoint only academic, however, since it is impossible that a circulation adequate for the needs of the myocardium could be carried on through a vessel the size of a vas vasis.

The Condition of the Heart.—The hearts in these two cases weighed, respectively, 328 and 285 grams. Both weights are perhaps slightly above normal for the individuals, but the measurements are essentially normal. The measurement of the aortic ring in Case 1 bears essentially the normal ratio to the size of the pulmonary ring. The aorta above had begun to dilate, however, whether due to a slight insufficiency of the relatively normal aortic valves, to the aortitis, or to both is a question. In Case 2 there was no evidence of aortic insufficiency, and the arch above the lesion was intact and not dilated.

The circulation to the heart muscle was apparently adequate under ordinary conditions in each case. No evidence of fatty change, active myocarditis or repair was found in either case. The histories indicate that the individuals were comfortable except under condition of stress; overeating in Case 1, sexual or other emotional stimulus in Case 2.

THE LITERATURE OF OBLITERATION OF THE CORONARY ORIFICES

Allbutt[3] says: "Among the hearts which Kanthack examined with me I remember one in particular which was notable in this respect, that not only were the coronary arteries calcified, but their orifices were so utterly obliterated that the very seat of them was undefinable; yet in so far as the microscope could tell us the myocardium was normal." Vaquez[4] cites a case in a youth of eighteen years, complaining of pain in the precordial region, provoked by exertion and extending toward the left shoulder, and in whom, following physical examination, "clinically the diagnosis of organic angina could be excluded." Several days later he died in a paroxysm of pain. "At the autopsy, to our surprise, we found that there was a diffuse aortitis of the ascending portion of the aorta. The lesions predominated in the suprasigmoid region, where they had caused a sort of puffiness of the internal coat, chiefly about the orifices of the coronary arteries, which, if not obliterated, were at least notably obstructed." Notable obstruction is not occlusion, as a study of a large series of syphilitic aortae demonstrates.

The case mentioned by Cabot[5] does not belong in this group.

An interesting case, not of closure of the coronary orifices but of obliteration of the vessels beyond the orifices, is reported by Rondeau.[6] A man of sixty years, who died of carcinomatosis, primary in the liver, was found at post-mortem examination to show: ". . . . obliteration of both coronary arteries by a cretaceous clot, which follows the principal divisions of the arteries of the heart." He comments: "In the presence of so long-standing alteration of the coronary arteries that it produced complete obliteration of these vessels, it is astonishing that neither were any cardiac disturbances observed during life, nor more extended and pronounced lesions of the cardiac musculature (some fat granules)."

THE CORONARY ARTERIES BEYOND THE AORTA

In the reported cases of coronary orifice occlusion, in which from the age of the patient and description of the lesions it is evident that the occlusion is due to syphilitic aortitis, the comment is practically constant that the coronary arteries beyond the occluded orifices are normal. Even in older individuals in whom one can suspect from the localization of the lesions in relation to the aorta that the original process was syphilitic, it is usual to find reports of normal coronary vessels or those showing only the senile type of sclerosis.

The rarity of syphilitic lesions in the primary coronary arteries and their main branches is one of the interesting peculiarities of this protean disease. The cerebral vessels, of similar caliber, are a favorite site for syphilitic processes, the coronaries rarely so.

The indefatigable Warthin[7] who has made exhaustive search of materials for the purpose of discovering evidence of syphilitic disease, and who found syphilitic processes in the pulmonary, iliac, femoral, popliteal, tibial, carotid and subclavian arteries, says: "Syphilis of the coronary arteries, in our experience, has been found much less frequently than anticipated from its frequent mention in the literature. Although myocardial lesions occur in practically every case of late syphilis, these are interstitial infiltrations and proliferations along the smallest capillaries between the heart muscle fibers, and the larger branches of the coronaries only rarely show lesions that can be recognized as syphilitic. In every case in our experience these have been of the nature of an arteritis with obliterating proliferation of the intima often associated with thrombosis. Secondary arteriosclerotic changes may follow the healing of these lesions, as elsewhere, but the syphilitic nature of the process can only be recognized in the early stages."

Many authorities fail to agree with Warthin about the frequency of syphilitic myocardial lesions, and the type of syphilitic obliteration of the larger branches of the coronary arteries associated with thrombosis has not been found by us.

Scott[8] says: ". . . . it is interesting to note that in spite of the active disease surrounding their orifices the coronary vessels themselves were seldom involved. When opened they presented a smooth normal surface."

Clawson and Bell[9] after discussing the narrowing or closure of the coronary orifices say: "As in the cases of aortic insufficiency coronary disease in these fifteen cases was rare, with the exception of syphilitic involvement of the orifices."

Our constant experience confirms these findings.

THE SUPPLY OF BLOOD TO THE CARDIAC CIRCULATION

It is quite clear in view of the findings that these two people were able to work and go about their daily lives with their coronary arteries completely occluded. The logical question therefore is, how did the heart muscle get sufficient blood supply to enable it to carry on its function efficiently? It is natural to look for additional coronary arteries but none could be found. One is left, therefore, with two possibilities. The first is that a potential source of blood exists in the anastomoses of the vasa vasorum of the aorta; but there was no enlargement of these channels, and, even had there been, it is only too obvious that the amount of blood which could be delivered through these vessels would not furnish blood enough to supply energy for the work of a single auricle. One is left then with the Thebesian veins as the only vessels capable of supplying blood to the muscle.

Vieussens[10] in 1706 showed a connection between the coronary arteries and the heart chambers, and two years later Thebesius[11] demonstrated a communication between the veins and the chambers of the heart. Many others have shown the presence of these vessels since that time, but F. H. Pratt[12] first demonstrated that it is possible to keep a mammalian heart beating by perfusing blood through the Thebesian vessels. His ingenious and conclusive experiments demonstrated for the first time the possibilities of a blood supply from the ventricles directly to the heart muscle. Since Pratt's experiments Crainicianu[13] (1922) has shown that when the coronary arteries were perfused with salt solution most of the perfusate escaped into the chambers of the heart and relatively little escaped via the coronary sinus. Wearn[14] confirmed the work of Crainicianu and found in some instances that as much as 90 per cent of the perfusate injected into the coronary arteries escaped directly into the heart chambers. Moreover, by serial histological sections a direct connection was shown to exist between the Thebesian openings in the ventricles and the veins and capillaries of the heart. Evidence was also brought forward to show a direct connection between the coronary arteries and the chambers of the heart.

With these findings in mind the channel of the blood from the ventricles to the heart muscle in the two cases reported in this paper is obviously through the Thebesian vessels. Nor is it surprising that these vessels are ample in size to supply the heart with a sufficient amount of blood when one examines the results of the experiments of Crainicianu and Wearn.

The histological study of the sections through the occluded area of the coronary arteries in these cases reveals a process of long standing—probably evolved over a period of months or longer. In view of this fact one is surprised to find so little evidence of heart disease in the histories of these patients. These people were able to work, and one of them did heavy work with both coronary arteries closed. It is difficult to devise any experiment that can demonstrate more conclusively the fact that under given conditions the Thebesian vessels can take over the rôle of the coronary arteries in supplying the heart muscle with blood.

It is the efficiency of the Thebesian circulation in this rôle, most likely, that explains the few clinical symptoms as well as the absence of heart failure. The same explanation almost certainly accounts for the absence of signs and symptoms of heart failure in those patients with advanced sclerosis which practically occludes both coronary arteries. In many instances these are first discovered by the pathologist.

The interesting point is that both syphilitic aortitis and sclerosis of the coronary arteries are relatively slow processes. The occlusion of the artery is gradual in each instance—so gradual, indeed, that the

Thebesian vessels have time to take over the new duty and readjust themselves to it. The element of time is apparently a very important factor.

Nowhere in the body is the adaptability of the human mechanism better illustrated than in the capacity of the heart, while functioning at full speed, to effect a complete revolution in the cardiac circulation, provided that the need for the change is brought about gradually.

SUMMARY

Two cases of essential closure of both coronary orifices are reported. The lesions indicate a slowly progressive process which has probably taken months at least to reach the point of essentially complete closure. No evidences of fatty change, myocarditis or repair were found in the heart muscle.

The only adequate explanation of the ability of these patients to live and work rests upon a belief that the Thebesian veins have supplied the compensatory circulation necessary for the functioning of the heart muscle.

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RECIPROCAL BEATING OF THE HEART; AN ELECTROCARDIOGRAPHIC AND PHARMACOLOGICAL STUDY*

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RECIPROCAL beating of the heart is a disturbance of unusual interest inasmuch as it is one of the few forms of bigeminy in which the mechanism is apparent. The four cases reported in this communication presented certain exceptional characteristics which appear to add to our knowledge of this disorder. In one case the disturbance was sufficiently prolonged to permit extensive pharmacological study.

RÉSUMÉ OF THE LITERATURE

Reciprocal beating of the heart was first described by Mines in 1913.[1] He showed that a single stimulus to an auricle-ventricle preparation from the electric ray or to a ventricle-bulbus preparation from the frog may provoke a continuously circulating excitation wave, the auricular contraction evoking a ventricular response and the ventricular contraction, an auricular response. Although several clinical examples of a disorder of this type were reported, the reciprocal nature of the mechanism was first noted by White in 1915.[2] The electrocardiographic tracings of White's case showed atrio-ventricular rhythm, the ventricle beating first and being followed at an interval by an auricular beat. When the R-P interval widened to a certain critical value, the auricular beat gave rise to a second ventricular response. The phenomena described by Mines and by White differ only in degree, the reciprocal beats of the auricle and ventricle as described by Mines continuing indefinitely, while in the clinical examples reported by White, the mechanism terminated abruptly after the second ventricular response. Since 1915 similar instances have been reported by White,[3] Gallavardin and Gravier,[4] Bishop[5] and Dock.[6] The condition was first termed reciprocal rhythm by Drury[7] who observed this type of disorder in a patient with paroxysmal tachycardia of A-V nodal origin. An instance of reciprocal beating in which the auricular contraction gave rise to a ventricular response, followed in turn by a second auricular response, recently has been reported by Wolferth and McMillan.[8]

CASE I. (C.W.)

The patient was a colored widower, 57 years of age, who entered the hospital May 22, 1928 complaining of shortness of breath. He had contracted

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syphilis about 20 years previously. Six months before entry he was awakened at night by severe precordial pain which persisted for three days and then suddenly disappeared. Three months before entry he noted the onset of dyspnea and a persistent productive cough. One week before entry swelling of the legs developed.

Physical Examination showed a fairly well developed, moderately orthopneic colored man. The pupils were slightly irregular, and reacted sluggishly to light and accommodation. The veins of the neck were markedly engorged. Numerous moist râles were heard everywhere over both lungs except at the bases where the physical signs of fluid were elicited. The heart was greatly enlarged both downward and to the left. The heart sounds were of poor quality; the rhythm was regular except for an extrasystole every three or four beats. There was a blowing systolic murmur at the apex transmitted to the axilla. The peripheral vessels were markedly sclerosed and tortuous. The blood pressure was 190 mm. Hg. systolic; 112 mm. Hg. diastolic. Signs of free fluid in the abdomen were present. The liver was greatly enlarged. There was marked pitting edema of the legs, thighs and back. The Kahn and Wassermann reactions were positive.

The clinical diagnoses were hypertension, myocardial failure, syphilis, generalized arteriosclerosis, hydrothorax (right) and possible coronary occlusion. The first electrocardiogram was taken after the patient had received full doses of digitalis and showed reciprocal rhythm. All electrocardiograms described below were taken after digitalis had been omitted for eight days.

Cardiac Mechanism.—The control tracings of this patient (Figure 1) show atrio-ventricular rhythm with coupling every third or fourth beat, without evidence of independent auricular activity. The origin of the unusual rhythm is either in the A-V node or in the bundle of His above the bifurcation, for the ventricular complexes are of the supraventricular type. Each ventricular beat gives rise, by retrograde conduction, to an auricular contraction represented in the tracings by diphasic P-waves. In most of the reported cases of A-V rhythm, the retrograde P deflection falls clear of the ventricular deflection and is almost always related in a constant manner, the Q-P interval remaining constant. In this case, however, the relation between the initial ventricular deflections and the consequent auricular deflections is constantly changing owing to retrograde heart-block, the Q-P interval gradually increasing from 0.12 seconds in cycle A to 0.16 seconds in cycle B, and finally to 0.26 seconds in cycle C. In cycle C the Q-P interval is sufficiently great to enable the ventricle to recover from its refractory phase. The auricular wave therefore re-enters and excites another ventricular response, Y. The gradual increase in the Q-P interval signifies an increasing delay in retrograde conduction and is analogous to the gradual increase in the P-R interval seen more frequently in downward conduction in heart-block.

In all the many tracings observed, a premature beat occurred only when the Q-P interval was at least 0.26 seconds. The longest Q-P interval not followed by a premature ventricular response reached a value of 0.20 seconds. The refractory period of the ventricle in this case may therefore be placed within the limits of from 0.20 to 0.26

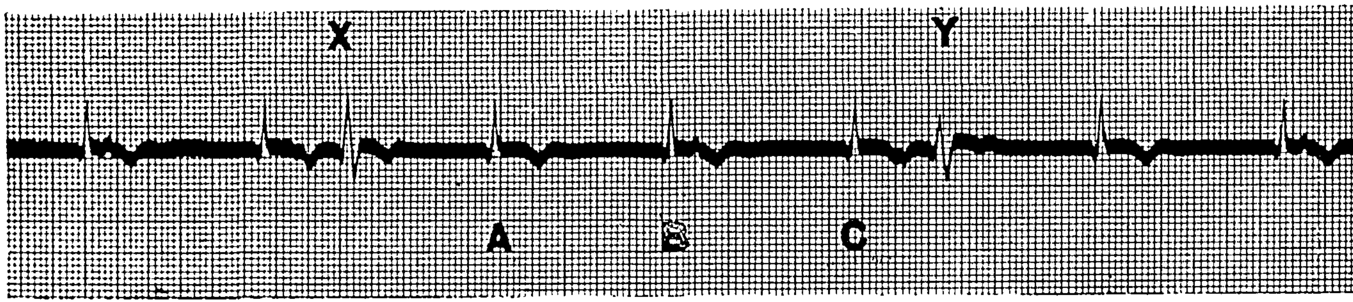

Fig. 1.—Case I. Lead II. Atrio-ventricular rhythm with retrograde heart-block. The retrograde P-waves are followed by a second ventricular response at X and Y.

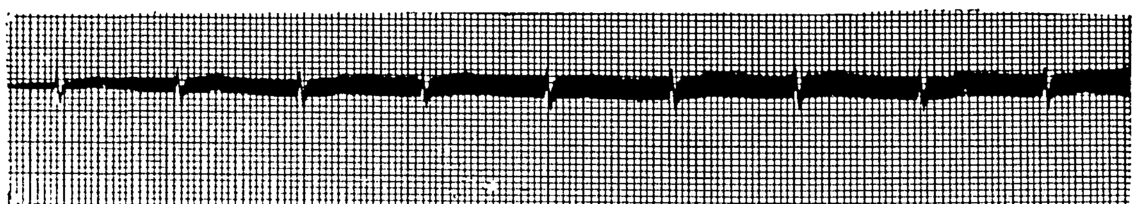

Fig. 2.—Case I. Lead II. Electrocardiographic tracings after 0.002 gm. atropine subcutaneously. Atrio-ventricular rhythm with abolition of reciprocal rhythm. Standardization was difficult because of high resistance.

seconds. The interval from the extra re-entrant beat to the next normal beat was approximately the same as between the usual nodal beats. This time relation is similar to that observed in patients with sino-auricular rhythm and auricular extrasystoles.

It is interesting to note that the Q-P interval was 0.26 seconds, whereas the P-R interval of the reciprocal beat was 0.28 seconds. The degree of block to retrograde conduction in this instance is approximately the same as that to downward conduction. This finding is exceptional, and is in contrast to that observed by White[2] in one case in which the Q-P interval was longer than the P-R interval,—0.378 seconds as compared with 0.24 seconds in one of the digitalis couples, and 0.376 seconds as compared with 0.289 seconds in one of the vagal pressure couples. As in our case, and in the instance of paroxysmal tachycardia of A-V origin reported by Drury,[7] the reciprocal ventricular beat appeared only when the Q-P interval exceeded a certain interval.

The constancy of the electrocardiographic phenomena displayed by the patient afforded an exceptional opportunity to study more intimately the mechanism and so the following observations were made.

THE EFFECT OF EXERCISE

After exercise, the ventricular rate rose from 79 to 94, falling to 82, two minutes after the completion of exercise, and to 76, five minutes after the completion of exercise. Exercise completely abolished the reciprocal beats so that the rhythm became regular. Examination of the tracings indicates that this change was due to the fact that the Q-P interval became shorter and so was not sufficiently great to permit the A-V node to recover from its refractory phase and transmit the re-entrant wave. The tracing was similar to that observed after atropine (Figure 2). The shortening of the Q-P interval was doubtless due to the inhibition of the vagus nerve which occurs on exercise[9] and is analogous to the disappearance of reciprocal rhythm after atropine observed by Bishop.[5] It is significant that in the case of atrio-ventricular rhythm observed by Gallavardin and Gravier,[4] reciprocal rhythm was present only when the vagus nerve was stimulated by pressure. Interruption of reciprocal rhythm by exercise was also observed in a patient studied by White.[3]

THE EFFECT OF VAGAL PRESSURE

In the absence of vagal pressure, reciprocal beats occurred every third or fourth cycle. Either right or left vagal pressure lengthened the Q-P interval so that the Q-P interval of the first returning cycle was 0.12 seconds, of the second cycle, 0.30 seconds. The latter auricular impulse re-entered and excited a second reciprocal ventricular

beat. A reciprocal ventricular beat consequently occurred every second cycle. The increased number of reciprocal beats led to a slight rise in the ventricular rate.

The P-R interval of the reciprocal beat was 0.16 seconds, instead of 0.28 seconds as in the control records. This shortening of P-R was probably due to more complete recovery of the A-V node during the increased Q-P interval. It is of interest that the converse of this situation has likewise been observed, that is to say, with shortening of the Q-P interval and a lessened opportunity for the A-V node to recover, the P-R interval of the re-entrant beat becomes lengthened. This inverse relation between the Q-P and P-R intervals was noted by Sherf and Shookhoff[10] experimentally and is in accord with observations by White.[3]

THE EFFECT OF EPINEPHRIN

The administration of 0.5 c.c. of a 1:1000 solution of epinephrin intramuscularly did not abolish the reciprocal rhythm. The Q-P and P-R intervals were not altered. An additional 0.5 c.c., 12 minutes later, produced no further changes. These observations indicate that the disappearance of reciprocal beats after exercise was not due to stimulation of the sympathetic nerves.

THE EFFECT OF PHYSOSTIGMINE

One milligram of physostigmine was injected subcutaneously, and electrocardiograms were taken at five minute intervals for thirty minutes, after which two additional milligrams were given. It was thought that physostigmine, by stimulating the vagus, might produce more frequent reciprocal beats. No such effect was observed, however.

THE EFFECT OF ATROPINE

The absence of any effect by epinephrin suggested that the disappearance of the reciprocal beats on exercise was due to the inhibition of the vagus.[9] To test this possibility, two milligrams of atropine sulphate were given subcutaneously and electrocardiograms were taken at frequent intervals during the following half hour. Atropine completely abolished the reciprocal rhythm (Figure 2) by shortening the Q-P interval to 0.12 seconds or less. No evidence of independent sinoauricular activity could be seen in any tracing.

This effect of atropine in abolishing reciprocal rhythm was noted by Bishop[5] but was absent in the case reported by Dock.[6] In the case reported by White in 1921,[2] atropine sulphate failed to affect the bigeminal rhythm because the Q-P interval was not sufficiently decreased.

Frequent tracings were taken during the following days of the patient's life. The amplitude of the QRS complex lessened conspicu-

ously and the cardiac rate dropped to 40 per minute with reciprocal beats following each nodal beat. In several tracings questionable extra ventricular systoles were observed.

COMMENT. Reciprocal beating of the heart in this patient seemed to be influenced mainly by vagal hypertonicity for, while epinephrin failed to affect the rhythm, both atropine and exercise completely abolished the reciprocal beats. The more frequent occurrence of reciprocal beats on vagal pressure is in accord with these observations. We are unable to explain the absence of any effect by physostigmine.

Similar to nearly all previously observed cases of reciprocal rhythm, the second ventricular complexes were aberrant in form. This is presumably due to transmission of the impulse downward during the partial refractory phase of the ventricle.

In reciprocal rhythm the retrograde P-waves are excited by the preceding ventricular beats so that, if the ventricular rhythm is regular, the retrograde P-waves will likewise be in a somewhat regular relationship to each other. It may be thought that the tracings of this patient might be otherwise interpreted as an instance of complete auriculo-ventricular dissociation, the auricles beating at a rate of 50 per minute and the P-waves, when they fell in a certain phase of the diastolic period, occasionally giving rise to ventricular beats. The following considerations weigh against the possibility of an independent auricular rhythm. (1) The P-waves were more closely related to the preceding ventricular complexes than to each other. (2) Exercise failed to cause a significant increase in the auricular rate. (3) Vagal pressure did not slow the auricular rate. (4) Atropine was without effect on the auricular rate. (5) The abolition of the bigeminy by atropine and exercise and the increased frequency of the disturbance in rhythm on vagal pressure conform to the previous observations on reciprocal beating of the heart and are inexplicable according to the other interpretation.

CASE II. (F.S.) The patient was a white widower, 55 years of age, who entered the hospital September 8, 1925 complaining of swelling of the legs. His past history was irrelevant. He had felt well until two years before admission when he noted gradually increasing breathlessness on exertion. One year before admission he noticed occasional swelling about the ankles. Four weeks before admission the symptoms became more marked and he was troubled by a productive cough. Four days before admission he was forced to discontinue work.

On *physical examination* the antero-posterior diameter of the chest appeared considerably increased. The percussion note was everywhere hyperresonant. There was a moderate number of medium moist râles at both bases. Expiration was prolonged. The cardiac borders could not be percussed out because of the hyperresonance of the chest. The heart sounds were distant, and coupled rhythm could be heard. No murmurs were audible. The peripheral vessels were moderately thickened and tortuous. The blood pressure was 130 mm. of mercury, systolic; 80 mm. diastolic. The tender edge of the liver was palpable 4 cm. below the costal

margin. There was conspicuous pitting edema of the legs and genitalia. The reflexes were normal. The Wassermann reaction of the blood was negative. The electrocardiograms described below were taken after the patient had been fully digitalized. The patient's condition gradually improved, and he was able to leave the hospital October 12, 1925.

The diagnoses were *generalized arteriosclerosis, myocardial failure and pulmonary emphysema.*

Cardiac Mechanism.—The electrocardiographic tracings of this patient show atrio-ventricular rhythm with right bundle-branch block (Fig. 3). As in Case I, reciprocal rhythm is clearly present. In the first three pairs of Lead I (Figure 3), the Q-P intervals are approximately 0.36 seconds, while the P-R intervals of the reciprocal beats are approximately 0.32 seconds. Downward conduction is evidently easier than upward or retrograde conduction, a relation similarly observed in the case reported by White.[2] This also has been observed experimentally, the Vs-As of retrograde beats being longer than the As-Vs interval in the same animal.[10] The seventh cycle in Figure 3 is not followed by a re-entrant beat. Here the Q-P interval of 0.32 seconds evidently was insufficient to permit recovery of the A-V node. In Lead II (Figure 4) the R-P interval of the second ventricular complex is 0.36 seconds with a P-R interval of the reciprocal beat of 0.26 seconds. This relation is also present in the fourth and fifth cycles. The sixth ventricular complex is followed by a retrograde P-wave after an interval of 0.32 seconds, an interval which evidently was insufficient to enable the ventricle to recover from its refractory phase. In no place is there evidence of independent auricular activity, the P-waves always succeeding the ventricular deflection and in some instances being followed by a second ventricular complex.

CASE III. (D.J.T.) The patient was 55 years of age, and entered the hospital June 16, 1915. Nine months prior to admission he first experienced sharp, agonizing pain over the heart. The attacks of pain occurred at night and lasted four to five hours. Six weeks before entry to the hospital, breathlessness occurred on exertion. Ten days before admission edema of the legs developed.

Physical examination showed extreme dyspnea, orthopnea and cyanosis. Respiration was periodic. The peripheral vessels were tortuous and sclerosed. Medium and coarse moist râles were heard everywhere over both lung areas. The cardiac impulse was diffuse but not forcible and was maximal in the sixth interspace, 17 cm. to the left of the midsternal line. The sounds were of fair quality. The second aortic sound was louder than the second pulmonic sound and was somewhat accentuated. A definite protodiastolic gallop rhythm and occasional extrasystoles were heard. No murmurs were audible. The liver was moderately enlarged and slight edema of the feet and ankles was present. The blood pressure was 184 mm. of mercury, systolic, and 140 mm. diastolic. Electrocardiographic tracings on June 17 showed normal sinus rhythm. The tracings described below were taken after the patient had received 0.1 gram of digitalis leaves three times daily for 4 days. After rest in bed the patient improved and left the hospital, July 18, 1915. He died at home on February 17, 1916.

Fig. 3.—Case II. Lead I. Reciprocal rhythm is present in the first three pairs of beats with Q-P intervals of approximately 0.36 second, and P-R intervals of the reciprocal beats of approximately 0.32 second.

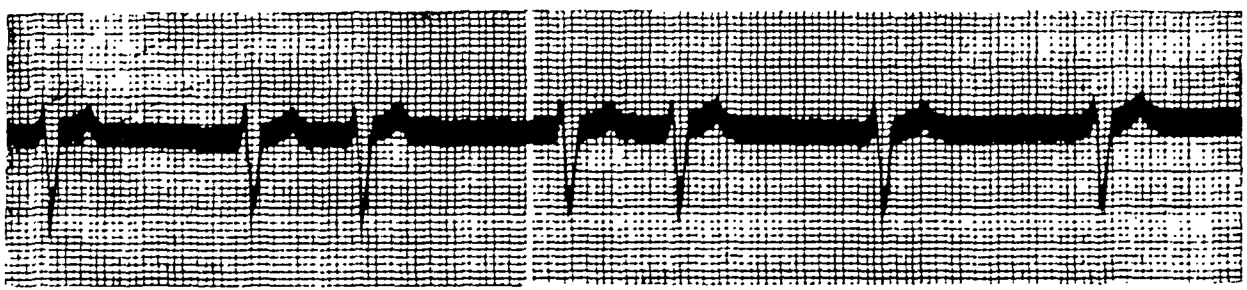

Fig. 4.—Case II. Lead II. Showing essentially the same features as the tracings of Fig. 3.

Cardiac Mechanism.—The tracings (Figures 5, and 6) in this case show reciprocal beating of the heart, with A-V nodal rhythm and retrograde heart-block. In Lead I, (Fig. 5) the R-P interval of cycle A is 0.12 seconds, of cycle B, 0.18 seconds and of cycle C, 0.40 seconds, the latter P-wave being followed by a ventricular response. In this lead, lead II (Figure 6), and lead III, the P-R interval of the reciprocal beats is much shorter than the immediately preceding Q-P interval. This is in contrast to the observation in Case I but is similar to the findings in Case II and in one of White's patients.[2]

CASE IV. (H.L.H.) The patient was 44 years of age, and entered the hospital, May 22, 1926 complaining of shortness of breath. Two years before admission he noticed dyspnea on exertion, and three weeks before admission swelling of the legs and distention of the abdomen appeared. *Physical examination* showed orthopnea and marked cyanosis, congestion of the lungs and free fluid in the chest and abdomen. The heart was greatly enlarged. The heart sounds were of poor quality and coupled rhythm was present. At the base the second aortic sound was absent and there was a loud rough systolic murmur transmitted upwards. A systolic thrill was palpable in the second right interspace. The peripheral vessels were moderately sclerosed and tortuous. The blood pressure was 113 mm. of mercury, systolic and 68 mm. diastolic. There was marked edema of the scrotum, thighs and legs. Examination of the blood including the Wassermann reaction showed no abnormalities.

The clinical diagnoses were *cardiac decompensation, aortic stenosis, chronic myocarditis, general anasarca.* The electrocardiographic tracings were taken before digitalis could have taken effect. The patient became rapidly worse and died within a few hours after admission to the hospital.

Post-mortem examination showed *chronic endocarditis, aortic stenosis, hypertrophy and dilatation of the heart, anasarca, bronchopneumonia and chronic passive congestion of the viscera.*

Cardiac Mechanism.—The tracings of this patient (Figure 7, Figure 8) show the most marked variations in retrograde block of any hitherto observed. These variations confirm in certain details the observations on the preceding three cases. The ventricular deflection of cycle A, in Figure 7, is preceded by an inverted P-wave. The ventricular deflection is of supraventricular origin. The occurrence of the P-wave before the ventricular deflection is evidently due to facilitation of the spread of the excitation wave upwards so that the auricular response occurs at an appreciable interval before spread of the excitation wave downwards over the ventricle (approximately 0.12 seconds in this instance). In cycle B passage of the excitation wave evidently encounters more difficulty, for the P-wave seems to be buried in the QRS deflection. In cycle C the P-wave follows the initial portions of the QRS deflections by approximately 0.12 seconds. The retrograde P-wave distorts the S-T interval and causes more marked inversion of the T-wave. In cycle D the R-P interval has increased to 0.28 seconds. The ventricle has evidently recovered from the absolute refractory stage for a ventricular response immediately follows the P-wave (cycle E). The aberrant form of this complex probably is due to the

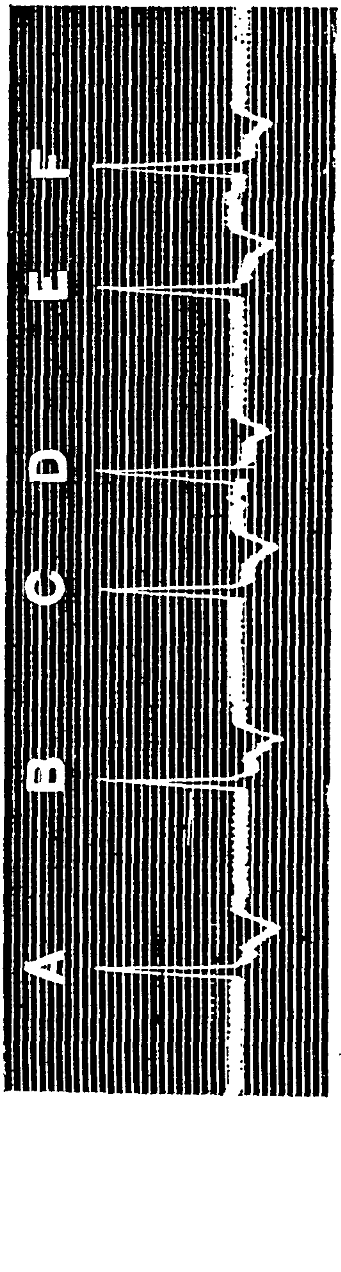

Fig. 5.—Case III. Lead I. Atrio-ventricular rhythm, partial retrograde heart-block and reciprocal beats at D and F.

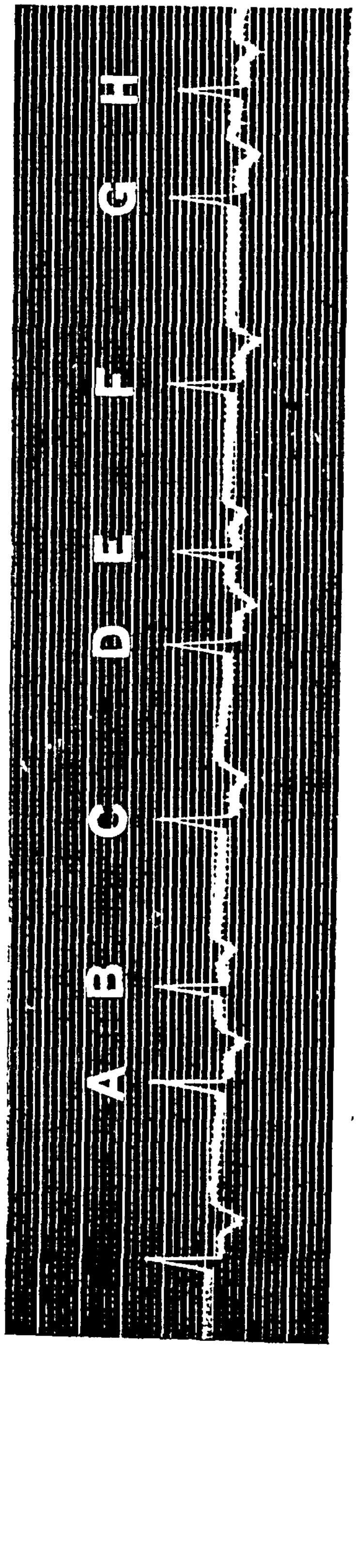

Fig. 6.—Case III. Lead II. Showing essentially the same features as Fig. 5.

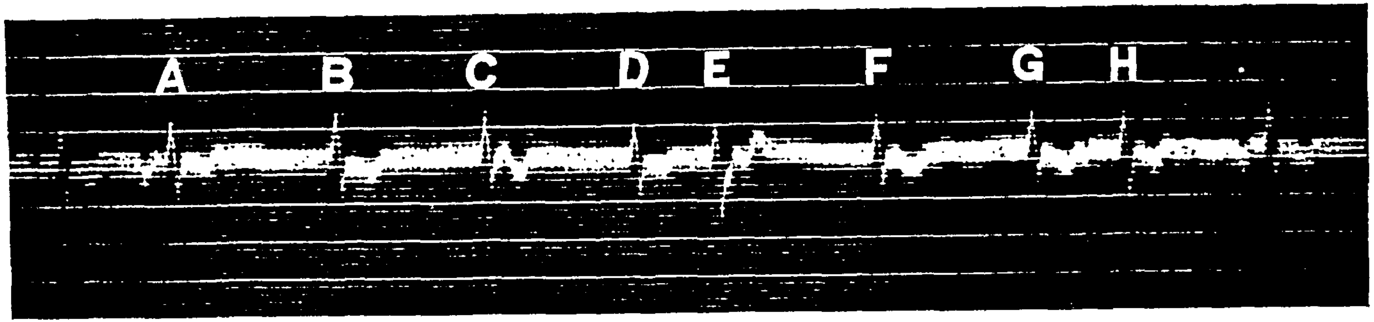

Fig 7.—Case IV. Lead II. In cycle A the inverted retrograde P-wave precedes the ventricular deflection. In succeeding cycles the P deflections appear progressively later in relation to the ventricular complex due to partial retrograde heart-block. Thus in cycle B the P-wave is evidently buried in the QRS deflection while in cycle C, it deforms the S-T interval. Finally in cycle D, the R-P interval is widened to such an extent that the P-wave falls sufficiently clear of the refractory phase of the ventricle to excite another ventricular response, cycle E. The aberrant form of the ventricular deflection of cycle E is evidently due to the fact that the ventricle is still in the partially refractory phase.

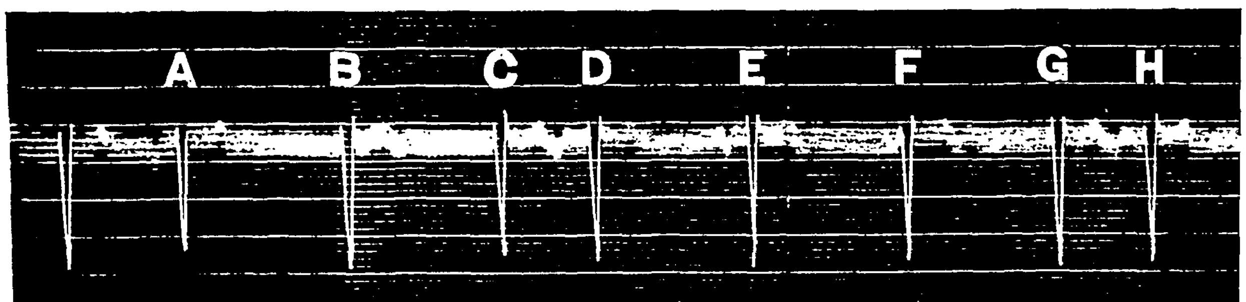

Fig. 8.—Case 4. Lead III. In cycle A, the sharply inverted retrograde P-wave precedes the ventricular deflection. In cycle B, the P-wave causes notching of the T-wave while in cycle C, it falls on the terminal portion of T and excites a second ventricular response. This chain of events is repeated in the remaining cycles of this tracing.

fact that the response occurred while the ventricle was still in the partial refractory phase. This interpretation is supported by cycles G and H. The R-P interval in cycle G is 0.04 seconds longer than in cycle D; the ventricle has had a longer period of time in which to recover and consequently the succeeding reciprocal cycle H beat is more nearly normal in outline.

Similar events are shown in Figure 8 which is a tracing from Lead III. In the first cycle following the previous reciprocal beat, the P-wave appears before the ventricular deflections. In cycle B, the P-wave depresses the S-T interval and causes notching of T. In cycle C the R-P interval is approximately 0.32 seconds, and a reciprocal beat of the heart follows. The degree of retrograde block shown in this case is not uniform so that reciprocal beats occur every third, fourth, or fifth cycle. As might have been expected with such varying R-P intervals, the P-R intervals likewise vary, the shorter R-P intervals being followed by longer P-R intervals of the reciprocal beats. The characteristic pairs of ventricular complexes with an inverted auricular deflection sandwiched between are seen in cycles C and D, and G and H.

SUMMARY

The clinical and electrocardiographic aspects of four cases of reciprocal beating of the heart are recorded and the nature of the abnormal mechanism is discussed.

In one case the disturbance was sufficiently prolonged to permit extensive pharmacological study. This study indicated that reciprocal beating was influenced mainly by vagal hypertonicity.

It is a pleasure to acknowledge our indebtedness to Dr. Henry A. Christian for the use of the records of the Peter Bent Brigham Hospital and to Dr. Samuel A. Levine for his helpful suggestions.

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THE MECHANISM OF TRANSITIONS FROM AURICULO-VENTRICULAR DISSOCIATION TO S-A RHYTHM; ITS RELATION TO THE THEORY OF PARASYSTOLE*

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BIGEMINAL rhythm has been the subject of considerable study, not only because it is intrinsically important, but also because knowledge of its mechanism may aid in understanding other cardiac irregularities such as paroxysmal tachycardia. At the present time there are two prevailing theories concerning the mechanism of coupled beats, the theory of re-entry and the theory of parasytole. According to the former theory, the second extra beat is excited by the re-entrant wave of the preceding normal systole. According to the theory of parasystole, the extra beat is not related to the normal systole, but is one of a series of impulses built up slowly and rhythmically by another independent center. The two impulse centers, the one normal, the other arising anew, are in the main independent but may not be completely so, for premature beats may be liberated from one center by the occasional receipt of an impulse from the other.

In a previous communication[1] four examples of coupled rhythm were reported in which the mechanism seemed explicable according to the theory of re-entry. The tracings showed atrio-ventricular rhythm with occasional coupled beats. An inverted or diphasic auricular complex was sandwiched between the two coupled beats. The mechanism of the disturbance was interpreted as follows. The impulses originated in the A-V node with propagation of the impulse upward over the auricles and downward into the ventricles. In succeeding cycles, ventricle-to-auricle conduction became more and more difficult because of retrograde partial heart-block, the auricular complex occurring progressively later in relation to the ventricular deflection until the Q-P interval was sufficiently great to allow recovery of the ventricle from its refractory phase. When the Q-P interval reached a certain critical value, the P-wave evidently re-entered the ventricle and excited a second ventricular response. The coupling displayed by the four cases was explicable, therefore, according to the theory of re-entry.

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The following two cases are examples of coupling, the mechanism of which seems clearly in accord with the other theory, the theory of parasystole.

CASE 1.

M.E.Y., was a colored widow of 47 years who had been in the hospital from May 19, 1925 to July 30, 1925. At that time she had complained of a productive cough and breathlessness of one month's duration. Physical examination showed essentially the same abnormalities as on the present admission except for scattered areas of consolidation in both lungs. The clinical diagnoses were bronchopneumonia, circulatory insufficiency and syphilis. With rest in bed and digitalis, she improved and felt fairly well for 4 months or until five months before the present entry when she noted the gradual onset of abdominal enlargement, breathlessness and palpitation of the heart. Because of these symptoms she was forced to enter the hospital again on April 28, 1926.

Physical examination showed a very dyspneic negress with slight edema of the face. The pupils were irregular and did not react to light. The heart was slightly enlarged to percussion. The underlying cardiac rhythm was regular, but was interrupted by an occasional extrasystole. There was a soft systolic murmur at the apex. The blood pressure was 230 mm. of mercury, systolic, and 115 mm. diastolic. The radial pulses were equal, synchronous and regular. Both lungs showed the physical signs of congestion and there was fluid at the bases of both lungs and in the abdomen. There was marked pitting edema over the tibiae and ankles. The Wassermann reaction was positive. The urine showed a trace of albumin with many waxy casts. The electrocardiographic tracings shown below (Figures 1 & 2) were taken May 17, 1926. During the preceding week the patient had taken a total of 1 gram of digitalis leaves. In spite of treatment, she grew progressively worse and died on June 21, 1926.

An autopsy was performed. The heart weighed 380 gms. On section the myocardium was found to be thickened and a moderate number of fibroid patches was present. The heart valves were normal. Numerous linear scars of the aorta were apparent just above the aortic valve and the intima was drawn into folds. The pathological diagnoses were chronic nephritis, tuberculosis of the left kidney, hypertrophy and dilatation of the heart, edema and atelectasis of lungs, chronic polyserositis, cirrhosis of liver, pyosalpinx, endometritis, syphilis and generalized arteriosclerosis.

Cardiac Mechanism.—The first four cycles of Figure 1 show normal sino-auricular rhythm, with P-R intervals of 0.15 seconds. The interauricular intervals between P_1, P_2, P_3, and P_4 are 0.70 second, 0.70 second and 0.71 second. The next auricular impulse, P_5, appears after 0.76 second. Before the impulse can be transmitted to the ventricle, the latter manifests its own inherent rhythm by escaping from sino-auricular control. P_5, P_6, P_7, and R_5, R_6, R_7, R_8 are unrelated, the electrocardiographic tracing showing complete auriculo-ventricular dissociation. Since the ventricular rate is faster than the auricular during this period of dissociation, the auricular deflections fall progressively later in relation to those of the ventricle. Hence, P_5 precedes R_5, while the diminution of S and the slightly increased height of R_6 indicate that P_6 is buried in the ventricular deflections. P_7 is

represented by the peaked S-T interval in R_7, while in R_8 the inversion of T is almost obliterated by the simultaneous occurrence of P_8. P_8 occurs 0.23 second following the onset of the preceding ventricular deflection, R_8, an interval sufficiently great to permit the ventricle to recover from its refractory phase. The auricular beat, P_8, consequently excites a premature ventricular response, R_9. The P-R interval of this coupled beat is 0.25 second, an interval somewhat greater than that during normal sinus rhythm. This increase in conduction time is probably due to transmission of the P-wave during the partial refractory phase of the A-V node.

The relatively prolonged P-R interval of P_8-R_9 allows the auricle to send another impulse, P_9, across the A-V node before the ventricle can build up its next impulse. P_9 consequently forces a ventricular response, R_{10}, after an R-R interval of only 0.66 second. The sequence of events then repeats itself, P_{10} stimulating a ventricular deflection R_{11}, while with R_{12} escape of the ventricle again becomes evident. The inherent rhythmicity of the ventricles in this tracing is higher than that of the auricles and so it may seem curious that the A-V node did not assume complete control of the auricles and ventricles. The failure of the A-V node to assume control is due to the blocking of all retrograde impulses from ventricle to auricle. The phenomenon of unidirectional block has been noted by other observers both clinically and experimentally and forms one of the important concepts about which the theory of parasystole is built. A similar form of coupling occurring in almost complete auriculo-ventricular dissociation has been observed, in a very few instances, by Hewlett,[2] White,[3] and Mobitz,[4] but so far as we are aware, no examples occurring with repeated transitions from S-A rhythm to complete auriculo-ventricular dissociation have previously been reported.

The case studied by Hewlett[2] showed complete dissociation except rarely when the auricular impulse descended upon the ventricle after a certain critical interval, and excited a premature beat of the ventricle. The P-R interval of the premature beats varied from 0.48 to 0.60 second. Auriculo-ventricular sequence was absent except for these rare beats. Reverse conduction from the ventricles to the auricle was so depressed that no retrograde P-waves were present. The case reported by White[3] was similar, complete dissociation being present except for rare beats showing A_s-V_s sequence. The P-R interval of the premature beats with transient auriculo-ventricular association was approximately 0.30 second. In all cases reported, the ventricular rate was higher than that of the auricles and reversed conduction from ventricles to auricles was absent.

Figure 2 is an electrocardiographic tracing, Lead III, from Case I. The mechanism of the irregularity is essentially the same as that shown in Lead I (Fig. 1). The tracing (Fig. 2) offers certain data

which corroborate the interpretation of the mechanism of the electrocardiogram of Lead I. P_1 is followed after an interval of 0.16 second by a normal ventricular response. Although P_2 precedes R_2 by 0.12 second, the ventricular deflection is of an aberrant type indicating that ventricular escape has occurred. P_2, P_3, P_4, P_5 and R_2, R_3, R_4, R_5, and R_6 show complete auriculo-ventricular dissociation. The ventricular rate is faster than the auricular so that the P-waves fall progressively later in relation to the ventricular complexes. During the period of complete dissociation the auricular impulses reach the ventricle while it is evidently still in the refractory phase. P_6 falls late enough, however, to incite a ventricular response, R_7. The contours of R_7 and R_8 indicate responses of the supraventricular type. Beginning with P_8 and R_9 complete dissociation is again evident. The previously described events then repeat themselves, P_{11} finally evoking a ventricular response, R_{13}, after a P-R interval of 0.28 second. Of the two P-waves, P_6 and P_{11}, which excite premature beats in this tracing, P_{11} occurs 0.07 second closer to the onset of the preceding ventricular deflection than P_6. The R-P interval of R_6-P_6 is 0.25 second, while the R-P interval of R_{12}-P_{11} is 0.18 seconds. The longer P-R interval of P_{11}-R_{13} is consequently to be explained by the P-wave reaching the ventricle earlier when the latter is more refractory. In Lead I the R_8-P_8 interval was 0.23 second and the P_8-R_9 interval 0.25 second, intervals closely similar to those of R_6-P_6 and P_6-R_7 in Lead III.

The tendency of the arrhythmia to repeat itself, to which the term *allorhythmia* has been applied, is of considerable interest. Kaufmann and Rothberger[5] observed that if the regularly beating auricle or ventricle of the dog or cat is exposed to a series of rhythmic shocks at any rate lower than the natural beat, a simple allorhythmia appears. This allorhythmia consists of premature beats occurring at certain regular intervals. It is the result of the regular interference with the building up of natural impulses by stimuli emanating from another independent source. The effective shock breaks down the stimulus material at the natural pacemaker prematurely and is followed by a pause of fixed length. As in Case I, the time relations between any two such rhythms leads to regular repetition of premature responses as soon as the time relation between the beat of one rhythm and the beat of the other rhythm reaches a certain critical value.[6]

The tracings of Figures 1 and 2 are clinical examples closely analogous to the phenomena observed by Kaufmann and Rothberger. The auricular impulses in these tracings are comparable to the series of rhythmic shocks to which the regularly beating ventricle is exposed. The time intervals of these clinical tracings are not as precise as those found experimentally, due probably to the influence of the extra cardiac nerves.

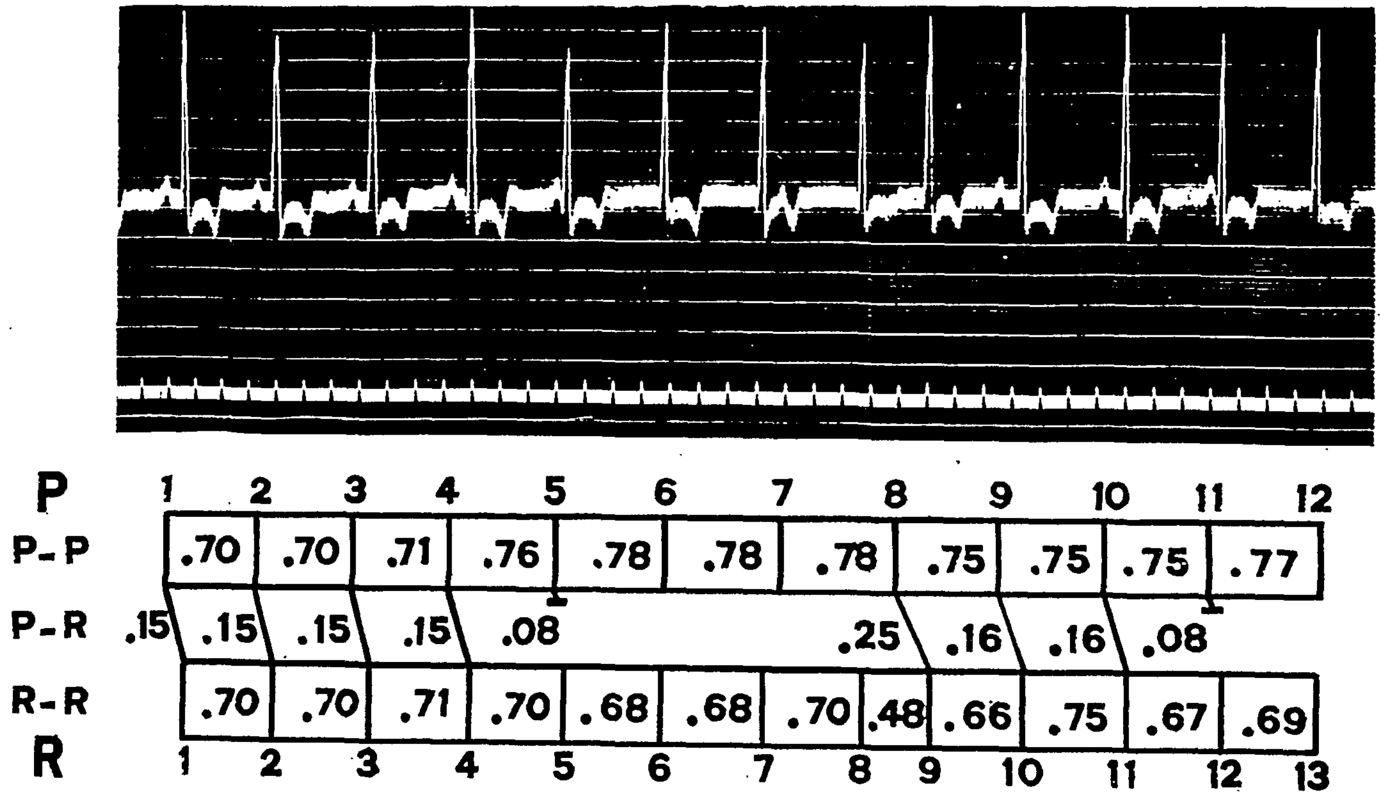

Fig. 1.—Lead I. Time is indicated in fifths of a second. In this and the following legends, P denotes the P-waves; *P-P*, the interauricular intervals; P-R, the interval between the beginning of the "P" and the "R" deflections; R-R, the inter-ventricular intervals; and R, the ventricular complexes. The first four cycles show normal sino-auricular rhythm. P_5, P_6, P_7, and R_5, R_6, R_7 show complete auriculo-ventricular dissociation. P_8 excites a premature ventricular response, R_9. Although there is no evidence of retrograde conduction, the premature response, R_9, is followed by quickening of the auricular rate which enables the sinus node to regain control.

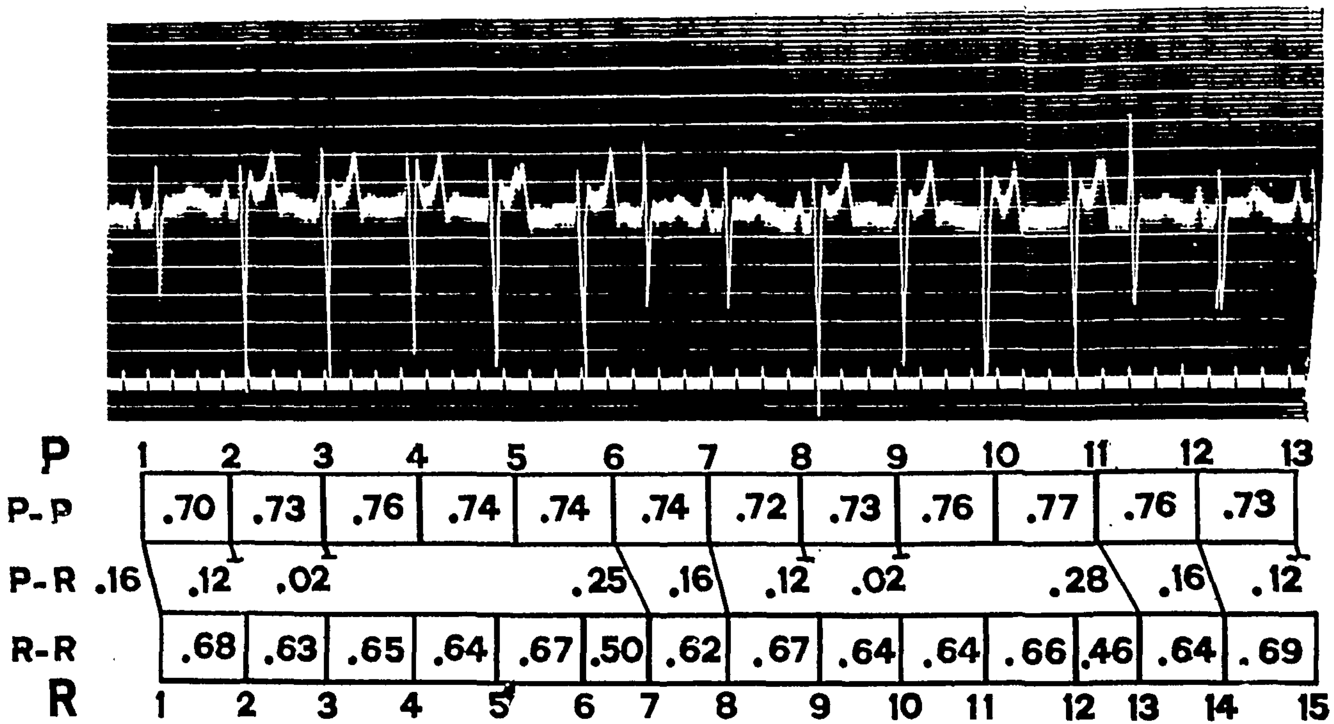

Fig. 2.—Lead III showing three transitions from sino-auricular rhythm to complete auriculo-ventricular dissociation. The relatively slow rate of the auricles prevents the occurrence of more than two successive auriculo-ventricular beats.

CASE II.

T.J.M., a white blacksmith's helper of 22 years, entered the hospital June 30, 1920. He felt well, until 10 days before admission, when he was forced to go to bed because of weakness, fatigue, and the onset of severe, dull substernal pain. There was no palpitation of the heart or swelling of the legs. Because of persistent pain and increasing weakness he decided to enter the hospital.

Physical examination showed orthopnea and marked venous pulsations in the neck. The heart was moderately enlarged downward and to the left. A rough systolic murmur transmitted into the great vessels of the neck and a soft blowing diastolic aortic murmur were heard over the conventional aortic area. The cardiac rhythm was regular except for a premature beat every 8 to 12 cycles. Both first and second sounds of the premature beat were audible. The radial pulses were equal, water hammer in type, and the rate was 60 per minute. The vessel walls were easily compressible. Duroziez's sign and a pistol-shot sound were heard over the femoral artery. The blood pressure was 190 mm. mercury, systolic and 0 mm. mercury diastolic. The lungs were clear and resonant throughout. The vital capacity of the lungs was 4000 c.c. Examinations of the urine and blood were repeatedly negative.

The diagnoses were chronic rheumatic valvular disease, mitral stenosis and insufficiency, aortic insufficiency and stenosis.

The patient responded readily to treatment, and rest in bed. He did not receive digitalis. The electrocardiographic tracings were taken on June 30, 1920. He was discharged July 10, 1920.

He was readmitted August 7, 1921. Physical examination showed essentially the same findings as previously with the exception of the signs of fluid at the bases of the lungs and marked pitting edema of both legs. The electrocardiographic tracings on this admission showed normal sinus rhythm. He died at home, October 13, 1921.

Cardiac Mechanism.—The cardiac mechanism in Figure 3 is similar to that present in Case I. P_1 excites a ventricular response, the transmission interval of 0.21 second, indicating delay in conduction. The inherent rhythmicity of the ventricles is greater than that of the auricles and leads to ventricular escape. P_2, P_3, P_4 and R_2, R_3, R_4 and R_5 show complete auriculo-ventricular dissociation. The relation between the auricular and ventricular beats is such that the auricular impulse occurs progressively later in relation to the ventricular impulses. The auricular impulses are not followed by ventricular responses because they descend upon the ventricles while the latter are evidently refractory. The onset of P_3, for example, precedes the onset of R_3 by 0.08 second, while the onset of P_4 occurs 0.13 second after the onset of R_4. The beginning of P_5 follows the initial deflections of R_5 by 0.22 second, an interval of time sufficiently great to permit ventricular response after a transmission interval of 0.44 second. This increase in the P-R interval of P_5-R_6 indicates partial refractoriness of the A-V node. The forced beat evidently destroys the immature impulse forming in the ventricle and a new impulse is then built up at the usual rate. Following the ventricular response, R_6, the next ventricular beat might have been expected after an interval of approximately 1.13 seconds. But before the ventricle can build up

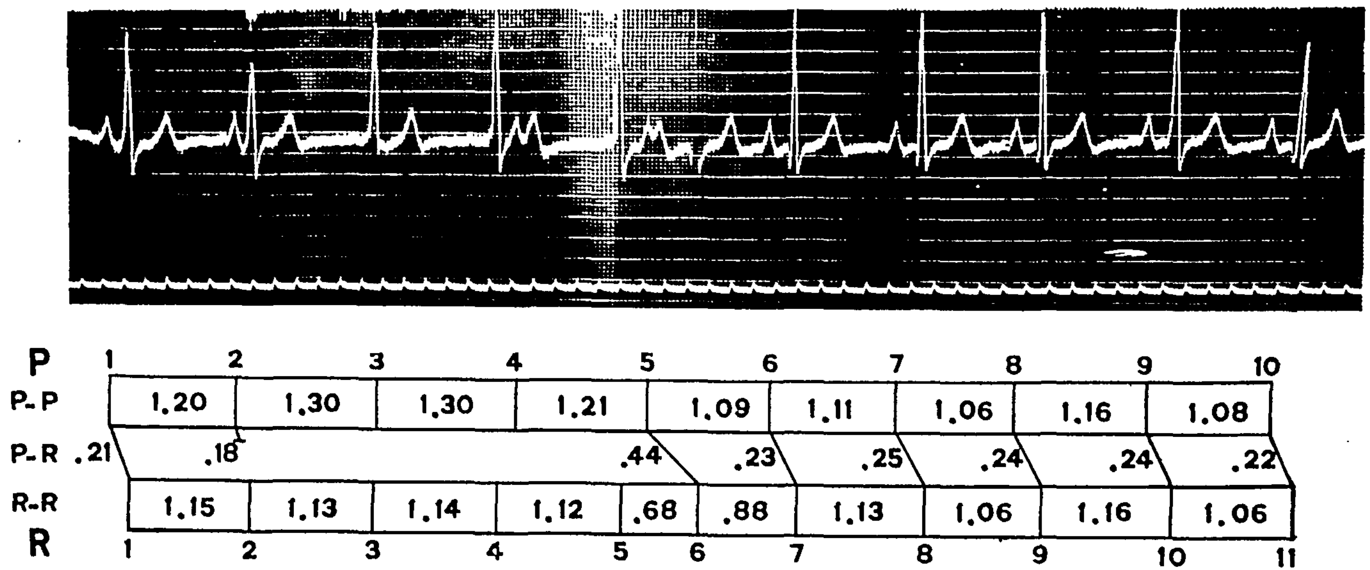

Fig. 3.—Lead II. P_1 excites a ventricular response but P_2, P_3, P_4, and R_2, R_3, R_4, R_5 show complete auriculo-ventricular dissociation. P_5 excites a ventricular response, R_6, and is followed by a quickening of the auricular rate enabling the S-A node to maintain control of the heart during immediately succeeding cycles.

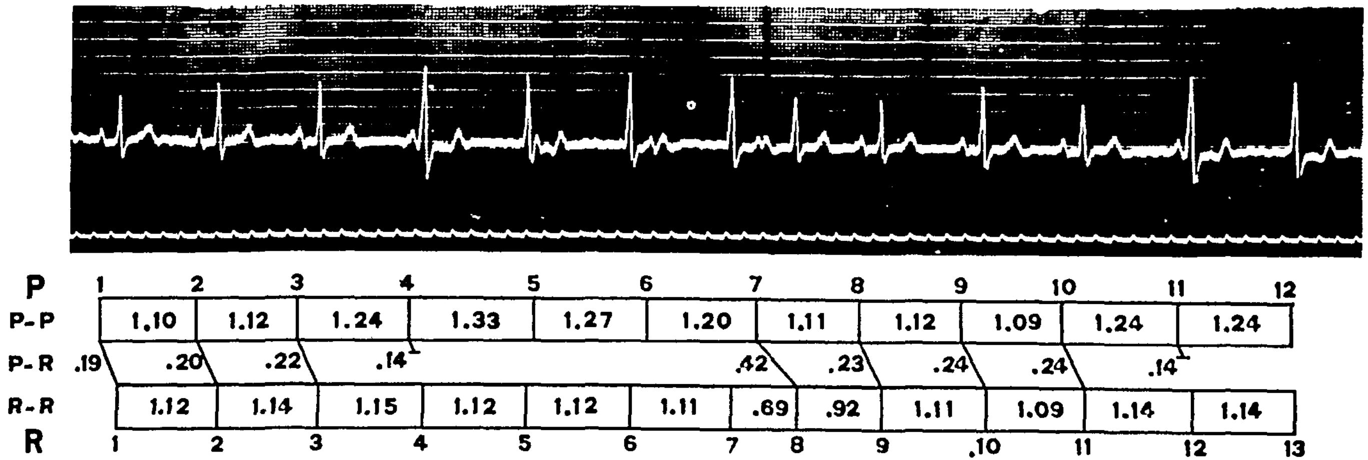

Fig. 4.—Lead III. Case II. Two transitions from S-A rhythm to complete auriculo-ventricular dissociation are present. The premature ventricular beat, R_8, excited by P_7, is coincident with a quickening of the auricular rate.

this impulse, the transmission of P_6, after an interval of only 0.88 second, forces a response R_7. The coupled beat, R_6, is coincident with a quickening of the auricular rate so that the latter approaches the rate of the ventricles. As in Case I, this faster auricular rate enables the S-A node to maintain control of the heart during immediately succeeding cycles. This effect of the ventricular contractions on the rate of the auricular contractions is somewhat surprising in view of the complete block to reversed conduction which was present during the period of complete auriculo-ventricular dissociation. This effect of the ventricle on the auricular rhythm has been noted in clinical examples of complete heart-block by Wilson and Robinson.[7] They observed that the interauricular interval period during which the ventricular systole fell was shorter than those which followed.

Figure 4 shows a tracing of Lead III of Case II. The first three P-waves, P_1, P_2 and P_3 incite normal QRS deflections. P_4, however, precedes R_4 by too short an interval to be responsible for the ventricular response. The aberrant form of the QRS deflections of R_4 is further evidence that escape of the ventricle has occurred. P_4, P_5 and P_6 represent auricular contractions which are entirely dissociated from ventricular deflections, R_4, R_5, R_6 and R_7. P_7, however, falls sufficiently clear of R_7 to excite a ventricular response, R_8, after a transmission interval of 0.42 second. The appearance of the premature coupled beat is coincident with a quickening of the auricular rate so that the S-A node regains and maintains control of the heart until P_{11}. The interauricular interval P_{10}-P_{11} is lengthened and complete dissociation again appears with P_{11}, P_{12} and R_{12}, R_{13}. The tracings of Case II show the same fundamental features as those of Case I. Both show inherent rhythmicity of the ventricles greater than that of the auricles; both show the phenomenon of unidirectional block. The etiology of the heart disease in Case I was syphilitic, in Case II, rheumatic. Both patients showed elevated systolic blood pressures. The abnormal mechanism occurred in Case I after moderate doses of digitalis while in Case II the phenomenon appeared without digitalis.

SUMMARY

1. Electrocardiographic tracings of two patients showing a rare form of bigeminy are described. Although a similar form of coupled rhythm occurring in almost complete auriculo-ventricular dissociation has been observed rarely, no instances occurring in repeated transitions from complete auriculo-ventricular dissociation to S-A rhythm have previously been reported.

2. The period of auriculo-ventricular dissociation was terminated by an A_s-V_s sequence when the auricular impulse descended to the ventricle after an interval of at least 0.46 second in Case I and of at least 0.68 second in Case II. Although reversed conduction from ven-

tricle to auricle was at all times absent, the premature ventricular response was invariably followed by quickening of the auricular rhythm, the S-A node gaining control of the heart for several beats. With subsequent slowing of the auricular rate, complete auriculo-ventricular dissociation again occurred and the cycle of events was repeated.

3. The abnormal mechanism occurred in one case after moderate doses of digitalis; in the other case, in the absence of digitalis medication.

4. The relation of the mechanism to the theory of parasystole is discussed.

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THE QUANTITATIVE ASPECTS AND DYNAMICS OF THE CIRCULATORY MECHANISM IN ARTERIAL HYPERTENSION*

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THE etiological causes of arterial hypertension are manifold. In that sense, arterial hypertension is not a disease entity. Its presence over a prolonged period of time, nevertheless, exerts such an important effect on the entire vascular system and on the functions of a number of organs in man, that it should not be considered so much a symptomatic manifestation as an important morbid state of the body. A number of studies are available in the literature on morphological changes in patients suffering from high arterial blood pressure of long duration. These studies fail to reveal either the etiology or the mechanism of the circulation in the presence of high arterial blood pressure. There is, moreover, a lack of quantitative evaluation of the cardiac work and of the peripheral circulation. The largest part of the available and conflicting information has been obtained from animals with experimentally induced high blood pressure,[1, 2, 3] or from observations of certain qualitative aspects of the circulation in man.[4]

THE PROBLEM

This investigation was undertaken with the hope of shedding light upon the state of the circulation in man in the presence of high blood pressure. Such knowledge may be of aid in the understanding of certain clinical manifestations of this condition and of its complications. A better knowledge of the physiology of hypertension may be of value also in revealing the etiological mechanisms of the disease and thus pave the way for sound therapy.

Reliable methods for the measurement of the dynamics of the circulation in man have not been available until recently. The results of the few investigations that have dealt with the functional aspects of the circulation are in conflict, partly because of the frequent unreliability of the methods used, and partly because of a lack of precise correlation between the clinical state of the patients and the observations made. Throughout the developmental stages of arterial hypertension, just as in other morbid states, continuous changes occur in the bodily functions.

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Without the clinical definition of the condition of the patient the laboratory observations lose their significance.

In the presence of persistent hypertension it is important to obtain knowledge of the functional state of the heart and of the peripheral circulation. Methods for the direct measurement of the work and energy consumption of the heart in man do not exist. An estimation of the efficiency and accomplishment of the heart is, nevertheless, possible through a measurement of the peripheral circulation provided that the function of the cardiac valves is normal. In the evaluation of the state of the peripheral circulation in hypertension the following factors are of primary significance: (1) the pressure gradients in the vascular circuit, (2) the cardiac output per unit of time and per beat, (3) the circulating blood volume, (4) the velocity of blood flow, (5) the viscosity of the blood, (6) the hemoglobin content of the blood, (7) the peripheral resistance of the vascular bed, (8) the relative distribution of blood between the lesser and greater circulation.

If the cardiovascular system is considered as a simple hydraulic system, then an abnormal increase in the circulating blood volume, in the cardiac output, in the peripheral resistance, or in the viscosity of blood would produce hypertension. In reality, however, a number of regulatory mechanisms are active in the body which prevent the development of hypertension under certain conditions. These regulatory functions may influence the circulation independently or in combination with each other. Because of the presence of these regulatory mechanisms, one can not foretell, on the basis of theoretical consideration, the state of the circulation in man. Similarly, the effect of one or two measured aspects of the circulation on a third undetermined factor can not always be predicted. Thus normal and pathological conditions of the cardiovascular system may exist with normal blood pressure, although the blood volume is increased, as occurs following increased fluid intake, in certain types of circulatory failure and in diabetes insipidus. In like manner, the cardiac output and the velocity of blood flow may increase considerably without elevation in the arterial pressure as, for example, takes place with muscular work, in the presence of anemia, and in hyperthyroidism. An increase in the peripheral resistance does not always predicate high blood pressure. This state of affairs may be observed in heart failure and in the presence of vascular spasm. Increased viscosity of the blood is often present with normal blood pressure as occurs in diabetes mellitus, shock, and polycythemia. In these conditions compensatory changes of regulatory functions of the body prevent an increase in blood pressure. The above mentioned examples clearly indicate that in order to obtain a knowledge of the dynamics of the circulation in hypertension it is essential that *several* of the circulatory functions should be measured *simultaneously*.

PLAN OF INVESTIGATION AND METHODS USED

Eleven of the patients with hypertension studied comprised one group who were in good physical condition, with normal capacity for work (Table I). The high arterial blood pressure was discovered either accidentally, or during a physical examination undertaken because of the presence of subjective sensations. In another group, composed of sixteen patients, the muscular activities were limited because of dyspnea and weakness on moderate exertion (Table II). In both groups there was clinical evidence that peripheral arteriosclerosis was either absent or slight. The kidney function was normal in a majority of the patients. Observations were made additionally on three patients with primary chronic nephritis and secondary high blood pressure (Table III). None of the patients of any group exhibited signs of failure of the circulation while under observation.

The aspects of the circulation studied and the methods used were as follows: The arterial blood pressure was measured by the Riva Rocci method, using either a mercury sphygmomanometer with the auscultatory method, or the graphic recording device of Tycos. Often the two procedures were employed simultaneously. In our experience, in normal individuals and in a majority of patients with hypertension, the two methods give approximately identical results. There are patients with hypertension, however, in whom the pressure obtained with the graphic method is considerably higher. The arteriolar and the capillary pressures were estimated by a modified Recklinghausen technique.[5] The method of Moritz and Tabora[6] was employed to obtain the venous pressure. Measurement of the cardiac output per minute and per beat was made by the method of Field, Bock, Gildea and Lathrop[7]; seven alveolar air and mixed venous blood samples being obtained for each determination. We feel that for comparative measurements this method is reliable. Either the Tissot or the Benedict-Roth method was used in calculating the basal metabolic rate. The circulating blood volume was measured according to the technique described by Keith, Rowntree, and Geraghty.[8] Estimation of the arm to face circulation time was made with histamine.[9] The mean velocity of the entire circulation was calculated by dividing the circulating blood volume by the cardiac output per minute. All tests were performed in post absorptive state and with the patient in prone position.

RESULTS

Tables I, II and III contain the results of the measurements of the cardiac output per minute and per beat, the oxygen consumption and carbon dioxide output, and other related measurements on 30 patients with hypertension. On 16 of the patients repeated measurements were performed at different intervals. In all 68 measurements were made.

TABLE I

MEASUREMENTS OF THE RATE OF BLOOD FLOW, THE MINUTE VOLUME OF THE RESPIRATION, AND THE BASAL METABOLIC RATE IN PATIENTS WITH ARTERIAL HYPERTENSION HAVING NORMAL CARDIAC FUNCTION

PATIENT	DATE	AGE YEARS	PULSE RATE PER MIN.	ARTERIAL BLOOD PRESSURE: SYSTOLIC MM. HG.	ARTERIAL BLOOD PRESSURE: DIASTOLIC MM. HG.	RESPIRATORY MINUTE VOLUME L.	CARBON DIOXIDE TENSION: ALVEOLAR MM. HG.	CARBON DIOXIDE TENSION: VIRTUAL VENOUS MM. HG.	CARBON DIOXIDE TENSION: DIFFERENCE MM. HG.	CO_2 OUTPUT PER MINUTE C.C.	CARDIAC OUTPUT PER MINUTE L.	CARDIAC OUTPUT PER 100 C.C. O_2 CONSUMPTION L.	CARDIAC OUTPUT PER BEAT C.C.	METABOLISM: RESPIRATORY QUOTIENT	METABOLISM: PER CENT	METABOLISM: CAL/HR./SQ.M.
1	9/14/28	47	55	175	106	8.1	35.9	43.0	7.1	181	5.9	2.6	108			
	9/17/28		59	176	101	8.6	34.2	43.6	9.4	207	5.1	2.0	86			
	9/18/28		66	156	95	12.4	35.1	44.6	9.5	273	6.6	2.2	96	0.922	+18.9	45.8
	9/20/28		64	147	84	12.8	36.8	46.3	9.5	325	7.7	2.2	119	0.953	+39.9	53.9
			63	142	82	11.8	38.5	47.2	8.7	273	7.2	2.4	112	0.920	+22.2	47.0
2	9/29/28	17	77	168	114	7.4	41.8	49.0	7.2	225	7.6	2.8	99	0.811	+ 1.9	43.8
			75	167	120	7.8	41.7	48.9	7.2	219	7.4	2.8	99	0.823	+ 0.3	43.1
3	11/ 6/28	41	83	184	125	5.0	40.7	47.2	6.5	146	5.4	2.9	64	0.785	+11.4	40.1
			80	200	130	5.7	39.3	47.2	7.9	139	4.1	2.3	51	0.778	+ 7.2	38.6
4	12/17/28	41	107	270	160	6.5	36.0	43.1	7.1	172	5.5	2.5	51	0.793	+18.0	42.5
			109			5.2	35.3	41.9	6.6	135	4.7	2.9	44			
5	2/11/29	54	87	175	90	7.5	42.7	50.2	7.5	272	8.9	2.7	102	0.836	+50.0	52.6
6	2/19/29	51	89	205	110	6.6	43.8	49.8	6.0	210	8.7	3.3	98	0.792	+25.7	44.0
7	3/ 6/29	31	97	220	120	8.8	32.2	41.3	9.1	244	5.6	1.9	58	0.812	+48.5	54.2
	3/14/29		94	230	120	8.2	32.2	41.6	9.4	196	4.3	1.6	46	0.734	+32.2	48.2
	3/21/29		74	220	130	11.2	24.3	30.9	6.6	231	7.5	2.9	102	0.885	+28.1	46.7
8	4/17/29	55	86	235	125	4.7	39.0	47.8	8.8	126	3.4	2.2	39	0.796	−18.7	30.5
9	5/15/29	50	78	170	110	7.2	41.1	49.3	8.2	271	8.0	2.7	103	0.906	+22.5	45.9
10	6/20/29	48	76	222	125	6.5	33.5	43.6	10.1	170	3.4	1.6	48	0.820	+ 2.5	39.5
11	9/ 6/29	34	74	180	105	6.8	34.1	40.1	6.0	213	8.0	2.8	108	0.739	+18.4	43.2

TABLE II

MEASUREMENTS OF THE RATE OF BLOOD FLOW, THE MINUTE VOLUME OF THE RESPIRATION, AND THE BASAL METABOLIC RATE IN PATIENTS WITH ARTERIAL HYPERTENSION HAVING IMPAIRED CARDIAC FUNCTION

				ARTERIAL BLOOD PRESSURE			CARBON DIOXIDE TENSION								METABOLISM	
PATIENT	DATE	AGE YEARS	PULSE RATE PER MIN.	SYSTOLIC MM. HG.	DIASTOLIC MM. HG.	RESPIRATORY MINUTE VOLUME L.	ALVEOLAR MM. HG.	VIRTUAL VENOUS MM. HG.	DIFFERENCE MM. HG.	CO_2 OUTPUT PER MINUTE C.C.	CARDIAC OUTPUT PER MINUTE L.	CARDIAC OUTPUT PER 100 C.C. O_2 CONSUMPTION L.	CARDIAC OUTPUT PER BEAT C.C.	RESPIRATORY QUOTIENT	PER CENT	CAL/HR./SQ.M.
12	8/29/28	54	94	218	148	8.6	37.9	44.6	6.7	226	8.3		86			
	8/31/28		85	180	130	7.6	38.0	45.6	7.6	183	5.9	2.3	69	0.720	+11.4	41.8
	9/ 3/28		85	195	139	7.5	37.6	44.1	6.5	188	6.7	2.7	78	0.762	+10.1	41.3
13	9/ 5/28	58	80	163	102	6.0	39.4	45.4	6.0	157	6.2	2.9	77	0.741	− 2.1	36.7
			84	156	97	6.3	37.4	44.6	7.2	161	5.2	2.5	62	0.758	− 1.1	37.1
	9/ 8/28		84	156	97	5.5	39.3	47.8	8.5	153	4.3	2.1	52	0.723	− 1.9	36.8
			82	154	97	6.5	40.4	47.7	7.3	164	5.5	2.5	66	0.721	+ 0.8	37.8
14	9/22/28	49	72	192	120	8.3	38.9	47.5	8.6	245	6.9	2.4	95	0.875	+15.5	44.5
			75	183	118	7.0	38.8	47.7	8.9	216	5.8	2.3	78	0.882	− 0.3	38.4
	9/25/28		68	182	117	8.2	41.3	50.1	8.8	223	6.1	2.5	90	0.922	− 1.8	37.8
			67	172	112	7.4	41.1	50.5	9.4	207	5.2	2.3	80	0.920	− 9.6	34.8
	9/28/28		66	190	117	7.7	39.3	47.1	7.8	210	6.5	2.6	100	0.833	+ 1.8	39.2
			63	188	118	6.8	38.3	47.4	9.1	184	4.8	2.1	77	0.790	− 5.5	36.4
	10/30/28		77	190	100	7.9	40.9	50.6	9.7	231	5.7	2.2	74	0.890	+ 4.9	40.4
	11/ 1/28		75	178	116	7.7	41.3	50.9	9.6	214	5.3	2.1	71	0.828	+ 3.6	39.9
15	10/ 2/28	55	50	237	137	5.0	39.9	46.4	6.5	139	5.2	3.2	104	0.843	−19.6	28.1
			54	227	130	5.2	38.6	46.1	7.5	148	4.6	2.5	85	0.803	− 8.9	31.9
	10/ 3/28		47	193	115	5.0	37.3	44.7	7.4	130	4.1	2.6	87	0.824	−23.1	26.9
			48	193	115	4.5	37.9	45.1	7.2	117	3.8	2.7	79	0.812	−30.0	24.5

TABLE II—CONT'D

PATIENT	DATE	AGE YEARS	PULSE RATE PER MIN.	ARTERIAL BLOOD PRESSURE SYSTOLIC MM. HG.	ARTERIAL BLOOD PRESSURE DIASTOLIC MM. HG.	RESPIRATORY MINUTE VOLUME L.	CARBON DIOXIDE TENSION ALVEOLAR MM. HG.	CARBON DIOXIDE TENSION VIRTUAL VENOUS MM. HG.	CARBON DIOXIDE TENSION DIFFERENCE MM. HG.	CO_2 OUTPUT PER MINUTE C.C.	CARDIAC OUTPUT PER MINUTE L.	CARDIAC OUTPUT PER 100 C.C. O_2 CONSUMPTION L.	CARDIAC OUTPUT PER BEAT C.C.	RESPIRATORY QUOTIENT	METABOLISM PER CENT	METABOLISM CAL/HR./SQ.M.
16	10/10/28	58	73	181	115	8.1	35.3	44.0	8.7	187	5.0	2.2	68	0.838	+ 2.9	38.6
			71	189	118	7.0	36.7	44.4	7.7	176	5.3	2.5	74	0.820	– 0.8	37.2
	10/15/28		72	178	115	8.1	36.5	46.5	10.0	221	5.3	1.9	75	0.800	+29.0	48.4
			72	182	116	7.4	37.5	45.0	7.5	199	6.2	2.4	85	0.760	+21.8	45.7
	10/23/28		75	181	112	6.7	36.7	44.8	8.1	200	5.8	2.5	78	0.862	+ 7.5	40.3
	10/25/28		68	180	112	6.0	36.4	45.0	8.6	182	4.9	2.5	72	0.922	– 6.9	34.9
	10/27/28		70	182	110	7.5	35.4	44.1	8.7	198	5.3	4.2	76			
17	11/ 5/28	77	32	270	65	8.1	33.0	39.5	6.5	138	4.5	2.4	142	0.725	– 3.9	34.1
	11/ 7/28		33	265	70	8.4	32.5	39.6	7.1	154	4.6	2.3	141	0.780	– 1.7	34.9
18	3/15/29	41	86	160	90	9.2	37.2	44.1	6.9	180	6.2	2.4	72	0.711	+15.3	41.5
	4/ 1/29		73	170	105	9.9	35.0	41.2	6.2	199	7.3	3.3	100	0.894	+ 1.1	36.4
19	3/19/29	48	100	210	112	6.5	44.2	54.0	9.8	198	4.8	1.8	48	0.725	+45.1	52.2
	3/23/29		84	204	112	6.5	38.3	47.5	9.2	169	4.4	1.8	53	0.685	+31.1	47.3
	5/28/29		90	250	135	5.8	38.0	50.0	12.0	166	3.3	1.5	36	0.744	+20.7	43.4
20	4/ 6/29	55	59	210	100	7.9	31.1	40.8	9.7	147	3.2	1.8	54	0.838	+ 7.1	37.5
21	4/16/29	39	74	218	115	5.9	39.7	48.0	8.3	167	4.9	2.3	66	0.774	– 3.0	35.4
	4/18/29		67	230	130	6.7	38.7	47.9	9.2	195	5.1	2.1	77	0.813	+ 7.4	39.2
22	4/29/29	18	101	170	112	8.8	45.2	53.1	7.9	234	7.1	2.9	71	0.940	+31.0	49.8
23	5/21/29	60	66	285	140	6.0	42.7	49.8	7.1	177	6.1	2.7	93	0.784	+ 7.1	36.4
	5/24/29		62	256	116	5.5	42.6	49.3	6.7	153	5.6	2.6	90	0.719	+ 1.0	34.3
24	6/ 5/29	65	81	241	120	8.5	35.9	43.7	7.8	214	6.3	2.5	78	0.849	+15.1	42.0
25	7/ 3/29	55	63	225	100	9.0	37.5	48.8	11.3	190	4.0	1.6	64	0.742	+ 5.5	39.5
26	7/ 9/29	55	68	182	98	7.9	42.5	49.3	6.8	211	7.6	2.8	111	0.786	+11.2	41.7
27	7/16/29	59	70	220	120	7.9	37.4	48.5	11.1	198	4.2	1.7	60	0.778	+18.1	44.3

Table IV presents the averaged data for the three groups of patients and the group of normal subjects. The average cardiac output of the hypertensive patients with normal cardiac function was identical with that of the normal group although the maximal variations were greater in the group of hypertensive patients. Considerable difference was found in the output of the various patients and also in the same patient at different times. The observations showed no definite correlation between the blood pressure and the cardiac output. Although the average cardiac output per minute was 1.0 liter lower in patients with impaired cardiac reserve than in patients with normal capacity for work, nevertheless, this difference in blood flow was less when the cardiac output was calculated per 100 c.c. of oxygen consumed. The difference between the alveolar and venous carbon dioxide tension, in its relation to the rate of blood flow, is an important index of the efficiency of the circulation. The average difference between the alveolar and virtual venous carbon dioxide tension was the same in the normal subjects and in patients with normal functional capacity. It is of interest that while the average cardiac output of the patients with impaired function was lower than normal, the carbon dioxide transportation was higher. The blood flow corresponding to the consumption of 100 c.c. of oxygen was 2.4 liters, while it was 2.7 liters in 13 control normal individuals. In some of the patients with increased basal metabolism the rate of blood flow per 100 c.c. of oxygen consumed was even lower. It was 1.8 and 1.5 liters in patient 19.

The average rate of the exchange of blood gases in the capillaries was increased in the patients with lowered cardiac reserve in comparison with the patients with a normal heart function. A similar behavior has been noted[10] in patients with rheumatic heart disease. Table V presents data concerning the circulatory blood volume, the mean velocity of the circulation, and the arm to face circulation time in the presence of hypertension. The circulating blood volume was within normal limits in patients with hypertension regardless of whether the functional capacity of the patient was normal or moderately limited. The mean velocity of the circulation was either within or slightly above the upper limit of normal.

The respiratory minute volume as indicated in Tables I, II, III and IV was normal; the respiratory rate was also normal. The average tidal air volume was 448 c.c. in the group of normal subjects, 419 c.c. in the group of patients with normal function, and 394 c.c. in the group with impaired function. We did not observe hypoventilation in hypertension as suggested by Rappaport.[11] The oxygen consumption was normal—that is to say, below + 15 per cent of basal metabolism in 19 patients, and was elevated in 11 patients.

Table VI presents the gradient of pressure from the arteries to the arterioles, capillaries and veins. Abnormally high pressure was found

TABLE III

MEASUREMENTS OF THE RATE OF BLOOD FLOW, THE MINUTE VOLUME OF THE RESPIRATION, AND THE BASAL METABOLIC RATE IN PATIENTS WITH ARTERIAL HYPERTENSION AND CHRONIC NEPHRITIS

				Arterial blood pressure			Carbon dioxide tension								Metabolism	
Patient	Date	Age years	Pulse rate per min.	Systolic mm. Hg.	Diastolic mm. Hg.	Respiratory minute volume L.	Alveolar mm. Hg.	Virtual venous mm. Hg.	Difference mm. Hg.	CO_2 output per minute c.c.	Cardiac output per minute L.	Cardiac output per 100 c.c. O_2 consumption L.	Cardiac output per beat c.c.	Respiratory quotient	Per cent	Cal/hr./sq.m.
28	10/19/28	17	106	224	160	8.5	30.2	37.6	7.4	173	4.9	2.3	46	0.846	+10.0	44.0
			102	224	160	9.0	30.4	37.1	6.7	183	5.8	2.6	57	0.808	+17.2	46.9
29	2/16/29	29	105	230	140	6.9	35.6	42.2	6.6	180	6.2	3.1	59	0.916	+ 4.7	38.6
	2/18/29		90	250	145	8.0	34.0	43.2	9.2	169	3.8	1.8	42	0.829	+ 8.4	40.1
	2/26/29		100	164	110	6.4	34.1	43.6	9.5	151	3.5	1.8	35	0.792	+ 1.7	37.6
30	2/28/29	28	89	210	130	6.7	32.4	40.3	7.9	173	4.6	2.0	51	0.744	+19.7	44.3

TABLE IV

THE AVERAGE RATE OF BLOOD FLOW, THE MINUTE VOLUME OF THE RESPIRATION, AND THE BASAL METABOLIC RATE IN THE THREE GROUPS OF PATIENTS WITH ARTERIAL HYPERTENSION AND IN A GROUP OF CONTROL SUBJECTS

	AGE YEARS	ARTERIAL BLOOD PRESSURE		RESPIRATORY MINUTE VOLUME L.	CO_2 TENSION VIRTUAL VENOUS-ALVEOLAR MM. HG.	CARDIAC OUTPUT PER MINUTE L.	CARDIAC OUTPUT PER 100 C.C. O_2 CONSUMPTION L.	CARDIAC OUTPUT PER BEAT C.C.	METABOLISM	
		SYSTOLIC MM. HG.	DIASTOLIC MM. HG.						PER CENT	CAL/HR./SQ. M.
Arterial Hypertension with Normal Functional Capacity (11 Cases)	43	200	117	7.1	7.7	6.4	2.5	80	+17.6	43.6
Arterial Hypertension with Impaired Functional Capacity (16 Cases)	53	208	112	7.5	8.3	5.4	2.4	79	+ 8.2	39.8
Chronic Nephritis (3 Cases)	25	216	141	7.5	7.8	4.8	2.2	49	+12.7	42.8
Control Subjects (13 Cases)	27	106	69	6.7	7.7	6.4	2.7	97	+ 1.0	39.3

TABLE V

THE CIRCULATING BLOOD VOLUME, THE MEAN VELOCITY, AND THE ARM TO FACE VELOCITY OF THE CIRCULATION IN PATIENTS WITH ARTERIAL HYPERTENSION

PATIENT	DATE	WEIGHT KG.	HEMATOCRIT	PLASMA VOLUME C.C.	BLOOD VOLUME C.C.	BLOOD VOLUME PER CENT BODY WT.	MEAN VELOCITY SEC.	ARM-FACE VELOCITY SEC.	FUNCTIONAL CAPACITY
12	10/ 2/28	68.2	44.6	3309	5969	8.78	57		Impaired
13	10/ 4/28	61.4	37.9	2785	4485	7.95	51		Impaired
			41.6	2520	4370	7.13	49		
14	10/11/28	75.0	48.3	2946	5698	7.50	59		Impaired
	11/ 5/28		48.4	2513	4965	6.50	52		
2	10/ 5/28	61.3	40.9	3122	5264	8.53	42		Normal
15	10/ 2/28	64.1	42.8	2647	4632	7.13	63		Impaired
16	10/11/28	62.7	37.3	3415	5439	8.53	61		Impaired
17	11/ 5/28	55.9	35.3	2480	3865	6.93	51		Impaired
3	11/ 6/28	40.9	39.8	1987	3300	8.05	42		Normal
4	12/17/28	47.3	45.0	2525	4585	9.60	54	35	Normal
5	2/13/29	79.0	38.1	3015	4975	6.30	33		Normal
29	2/17/29	50.0	24.3	2170	2870	5.73	38		Impaired
	4/12/29	50.0	35.5	2315	3585	7.17	48		
6	2/19/29	65.5	38.4	3010	4890	7.48	34		Normal
30	2/28/29	50.0	30.1	2690	3900	7.80	51	20	Impaired
7	3/14/29	59.0	40.0	2020	3365	5.70	40		Normal
18	3/15/29	73.7	46.6	2040	3830	5.20	34	24	Impaired
19	3/19/29	50.9	47.5	2180	4155	8.16	58	26	Impaired
20	4/15/29	47.7	42.1	2220	3835	8.02	77		Impaired
21	4/16/29	78.2	44.6	2440	4400	5.63	53		Impaired
8	4/17/29	49.5	46.0	2060	3820	7.67	67		Normal
22	4/29/29	47.7	48.6	2100	4100	8.59	35		Impaired
9	5/15/29	77.2	46.5	2520	4705	6.10	35	21	Normal
23	5/21/29	70.5	46.0	2135	3960	5.62	40		Impaired
31	10/16/28	73.4	47.0	3430	6470	8.45			Impaired
32	10/24/28	66.0	41.2	2750	4675	7.20			Impaired
Average					4448	7.34	49	25	
Average Normal					5800	8.30	43	24	

to exist in the arteries and arterioles, whereas the pressure in the capillaries and veins was within the normal range. As has been noted before,[5] there is an abnormally great resistance in the arteriolar circuit of patients having arterial hypertension with high diastolic pressure.

DISCUSSION

A. *The Localization of the Peripheral Resistance in Arterial Hypertension.* In the presence of arterial hypertension a disproportion must exist between the cardiac output and the resistance offered the flow of blood through the peripheral vascular bed. Such disproportion may develop either because of increase in cardiac output and velocity of blood flow or because of change in the peripheral resistance. The findings presented above are in agreement with the findings of Lauter and Baumann[12] and Burwell and Smith,[13] but contrary to the observations of Liljestrand and Stenstrom[14] and Hayasaka.[15] They indicate that the cardiac output in the presence of high blood pressure is not above the upper limit of normal. According to our findings the cardiac output and the mean velocity of the circulation may be below normal in certain patients with apparently normal cardiac reserve. In the causation of hypertension, therefore, the disproportion is due to changes in the peripheral vascular bed. Whatever the nature of the morphological or functional vascular changes responsible for the development of high blood pressure may be, they must involve important and extensive areas. Changes in the larger or smaller vessels of a single organ alone cannot produce hypertension. It has been suggested[4] as a result of post-mortem studies of blood vessels that one of the important etiological factors in the causation of hypertension is the loss of elasticity of the walls of the larger arteries. It has been claimed[16, 17, 18, 19] that the active contractions or elastic rebound of the larger arteries during diastole plays an important rôle in the propulsion of blood. With the loss or reduction of the normal elasticity of the arteries, a compensatory higher initial blood pressure is essential to carry the blood through the capillary system with the optimal pressure and velocity. If this conception is correct, it would follow also, that the pressure in the precapillary vessels (arterioles) should be the same in hypertension as it is in normal individuals; or that an abnormally high pressure gradient should exist between the aorta and large arteries and the arterioles. This, however, is not the case. In a previous study[5] and in Table VI we have submitted evidence that in essential hypertension without marked arteriosclerosis, the abnormal fall in pressure is not between the large arteries and arterioles, but between the arterioles and the capillaries. In addition, we have shown that in normal individuals it is also between the arterioles and capillaries that the marked fall of pressure occurs. The drop in pressure may be as great as 80 mm. Hg. in normal individuals and 150 mm. Hg. in patients with hypertension. This finding is in harmony with the

observations of Landis[20, 21] that in the mesentery of the frog and of certain mammals the most significant peripheral resistance is offered by the arteriolar system, including the arteriolar ends of the capillaries.

The conception that the gradient of pressure between the arteriolar and capillary systems is abnormally high in arterial hypertension leads inevitably to the conclusion that the immediate cause of hypertension is an abnormal *accentuation of the normal physiological resistance of the arteriolar system.* This conclusion, of course, does not reveal the factors responsible for the increased arteriolar resistance.

TABLE VI

THE ARTERIAL, ARTERIOLAR, CAPILLARY AND VENOUS PRESSURES IN PATIENTS WITH ARTERIAL HYPERTENSION

PATIENT	DATE	ARTERIAL BLOOD PRESSURE SYST. MM. HG.	DIAST. MM. HG.	ARTE-*RIOLAR* PRESSURE MM. HG.	CAPILLARY PRESSURE MM. HG.	VENOUS PRESSURE MM. HG.	FUNCTIONAL CAPACITY
12	9/27/28	214	140	165	14	+ 6	Impaired
13	9/26/28	158	110	120	8	+ 5	Impaired
1	9/25/28	170	96	75	11		Normal
14	9/24/28	206	114	150	8	+ 2	Impaired
2	10/27/28	180	124	100	11	+ 8	Normal
16	10/11/28	184	118	100	13	+ 5	Impaired
17	11/ 5/28	270	65	130	9	+ 7	Impaired
3	11/ 6/28	180	120	150	11	+ 5	Normal
4	12/17/28	280	160	150	9	+ 9	Normal
30	2/28/29	210	130	90	21	+ 4	Impaired
18	3/15/29	160	90	110	14	+ 6	Impaired
7	3/18/29	230	120	130	11		Normal
19	3/19/29	210	112	110	12	+ 4	Impaired
20	4/15/29	215	90	120	18	+12	Impaired
21	4/24/29	185	120	110	12	+12	Impaired
9	5/15/29	170	110	130	14	+ 6	Normal
15	10/ 2/28	220	115			+ 5	Impaired
29	2/16/29	230	140	120	7	+ 2	Impaired
Average		204	115	121	12	+ 6	
Average Normal		126	64	55	8	+ 5	

B. *The Quantitative Aspect of the Arteriolar (Precapillary) Resistance in Arterial Hypertension.* In a rigid tubing system the relationship between pressure and stream is expressed according to Poiseuille's law,[22] which states that the amount of fluid streaming through a narrow tube is directly proportional to the fourth potential of the cross sectional area and to the pressure of the fluid; and indirectly proportional to the length of the tube.

$$V = \frac{K.P.D^4}{L}$$

V signifies the amount of fluid flowing through the tube in a unit of time; P, the pressure of the fluid; D, the cross sectional area of the tube; L, the length of the tube; K, a constant. Although, as Tiger-

stedt[23] has pointed out, it is questionable whether this law can be rigidly applied to the circulation, the error involved in such application cannot be large enough to change the general significance of the conclusions. If one considers that, as observed, the circulating blood volume in cases with hypertension is within normal limits, L, the length of the arterioles, is essentially unchanged; and V, the amount of fluid circulating through the vessels in a unit of time, is either normal or below normal—then it follows that because P, the arteriolar pressure, is high, D, the value for the cross sectional area of the arteriolar bed in hypertension, is smaller than in the normal condition.

In the causation of altered peripheral resistance of the circulation in hypertension, this change in the cross sectional area may well play the important rôle, for other factors, such as the relation between the blood stroma and plasma, as well as the viscosity of blood and the circulating blood volume, show no change from normal. If we, therefore, consider that the resistance of a tube system is directly proportionate to the length of the tube and indirectly to the cross section, it follows that the resistance being R:

$$R = \frac{P}{V}$$

According to our findings, the average mean blood pressure in the patients with arterial hypertension was 160 mm. Hg. (it ranged from 112 to 215). The average cardiac output was 5.8 liters. These findings would correspond to a resistance which may be expressed with an index of $\frac{160}{58} = 2.8$. In thirteen normal individuals, the average mean blood pressure was 87 mm. Hg. (it ranged from 62 to 114) and the average cardiac output was 6.4 liters, indicating a resistance index of $\frac{87}{64} = 1.3$. The peripheral circulation thus offered a resistance against the cardiac work which was about twice as great in the group of patients with hypertension as that present in normal individuals.

C. *The Cardiac Work in Arterial Hypertension.* As has been recognized[24] the cardiac energy required for maintenance of the velocity of blood flow at rest is slight (about 0.3 per cent of the total energy), as compared with the cardiac energy essential to overcome the peripheral resistance of the vessels. The velocity factor in the cardiac work, $\frac{W.V^2}{2\ G}$ (W representing the weight of the volume ejected; V, the mean velocity at the root of the aorta; and G, acceleration due to gravity), is negligible and the work of the heart, therefore, can be approximately estimated by the formula K.V.R in which V is the volume output of the heart; R, the mean peripheral or pulmonary arterial resistance in meters of blood, depending on whether the work of the left or the right side of the heart is calculated; and K, the specific gravity of

mercury. According to Frank[25] this method of calculation may involve an error of about 10 per cent. In view of the fact, however, that a more exact determination of the cardiac work in man is not available, this objection is only of theoretical significance. Therefore, assuming that the mean aortic pressure is 10 mm. higher than the brachial arterial pressure, the average work of the left side of the heart of the normal subjects studied is 8.38 Kg. m. per minute or 127 gm. m. per stroke. The work of the right side is about one-third of that of the left side. Inasmuch as skeletal muscle and the mammalian heart utilize only 20 to 25 per cent of the total energy for effective work[26] one may assume that the calories used by the heart of normal individuals must be about 4.5 times greater than the calories transposed into work; that is, the caloric consumption of the left side of the heart is 128 calories or 7.6 per cent of the caloric need for the total body metabolism.

Assuming that the relative fall of pressure from the aorta to the brachial artery in hypertension without marked arteriosclerosis is not greater than in the normal state,—an assumption justified from our previous observation[5] that the fall in pressure from the brachial artery to the arterioles of the skin is the same in hypertension as in normal conditions—it would follow that the work of the left side of the heart in the average hypertensive patient is 13.3 Kg. m. per minute, or 184 gm. m. per beat, and 798 Kg. m. per hour. This corresponds to about 45 calories per day; and if the normal and hypertensive patient's heart works with the same efficiency, it would follow that the caloric consumption of the left side of the heart in hypertension is about 202 calories or 10.7 per cent of the total metabolism.

The pressure in the pulmonary artery in patients with hypertension and normal cardiac function is not known. Certain morphological evidence, namely, the absence of arteriosclerosis in the pulmonary circuit[27] and the frequent lack of muscular hypertrophy of the right ventricle,[28] suggests that the pressure in the lesser circulation is essentially normal. Accordingly, the work of the right side of the heart in hypertension is not increased to any degree. The average work of the heart in arterial hypertension is therefore about 41 per cent higher than in normal individuals, although the peripheral resistance of the greater circuit is increased over 100 per cent. Whether or not the caloric requirement of the cardiac work is proportional to this increase in work depends on the comparative efficiency of the musculature of normal subjects and patients with arterial hypertension. The available evidence suggests that the economy of the work of the mammalian heart is below normal in the presence of acutely induced arterial hypertension.[29] In patients with hypertension the economy of the cardiac work cannot be studied at present.

D. *The Basal Metabolism and the Rate of Blood Flow in Arterial Hypertension.* The cause of the high basal metabolism observed in several of the patients is not clear. These patients showed symptoms of an abnormally active sympathetic nervous system: namely, shiny, slightly protruding eyes, wide pupils, a tendency to flush and perspire easily and to become disturbed or excited from trivial causes. In some, there was a slightly enlarged thyroid gland. In these patients with arterial hypertension and increased metabolism, in contrast to the usual hyperthyroid patients, the pulse rate, the velocity and the amount of blood flow were not increased in proportion to the metabolism. In cases 7, 19 and 27 the rate of blood flow was even below normal. Increased peripheral resistance may be responsible for the marked difference in the dynamics of the circulation between the patients with hypertension and high basal metabolic rate and patients with hyperthyroidism, high basal metabolic rate and normal blood pressure. Whether the increase in the peripheral resistance can be considered as a regulatory mechanism to prevent increased blood flow and increased cardiac rate in these patients can not be stated.

The clinical course of case 19 indicates that the metabolism may return to normal without change in the blood pressure. This patient showed a basal metabolism between 20 and 45 per cent above normal on repeated occasions. Further, besides clinical manifestations of hyperthyroidism, she showed a large firm thyroid gland so that a resection of the gland was performed. Following the operation the metabolism became normal and the patient's health improved distinctly. The systolic blood pressure, nevertheless, was 270 mm. Hg. and the diastolic pressure 140 mm. Hg., seven months after the operation.

E. *The Amount of Blood in the Lungs in the Presence of High Arterial Pressure.* The lesser circulation with its abundant capillary bed has an important influence on the function of the left ventricle and on the blood flow in the greater circulation. As stated by Starling:[30] "The distensibility of the lung capillaries may play an important part in enabling the lungs to act, so to speak, as a reservoir for the left side of the heart." Although the amount of blood in the lungs in the presence of hypertension is not known, it has been suggested that the reduced blood content of the lungs may be responsible for the elevated pressure in the peripheral arteries.[11]

The observations of G. N. Stewart on animals[31] and of Blumgart and Weiss[32, 33] on man indicate that the pulmonary circulation time is an index of the mean pulmonary velocity. According to the former investigator[31] the quantity of blood in the lungs, Q, equals $\frac{V.T}{60}$ where V is the volume of blood flow through the lungs per minute and T the mean pulmonary blood velocity in seconds. Measurements of the minute volume flow through the lungs and the pulmonary circulation time in

the same individuals by Blumgart and Weiss indicate that the calculated blood in the lungs was 884 c.c. or approximately 21 per cent of the total blood volume, when the average cardiac output was 7.6 liters and the average actual pulmonary circulation time was 8 seconds. In a larger series of normal subjects the actual pulmonary circulation time was 6.5 seconds.[32] Taking the average cardiac output, 6.38 liters, it was estimated that the amount of blood in the lungs was 589 c.c. or 11 per cent of the total blood volume. Considering that the average cardiac output was 6.4 liters in the control subjects, 589 c.c. is probably the approximate average amount of blood in the lungs of the normal group studied by us.

The average flow of blood through the lungs of patients with high blood pressure and normal cardiac function was 6.4 liters, the average circulating blood volume in the patients with normal function was 4363 c.c. or 7.5 per cent of the body weight. The average pulmonary circulation time in a group of 12 hypertensive patients with normal circulatory function was 10 seconds.[34] The amount of blood calculated according to the above formula is 1063 c.c. or about 24 per cent of the total blood volume. The amount of blood in the lungs of patients with hypertension and normal functional capacity is therefore greater than that of normal control individuals. These observations do not lend support to the hypothesis that reduced capillary bed of the lesser circulation is responsible for the development of high arterial blood pressure. Therefore, neither decreased volume of blood in the lungs nor altered respiration can be held responsible for the development of high arterial blood pressure.

The finding of relatively high blood content of the lungs in patients with arterial hypertension is in harmony with observations on animals. Fühner and Starling[35] working with the heart-lung preparation noted that every elevation of the systemic pressure produced increase of pressure in the left auricle and in the pulmonary artery. Coetta and Stäubli[36] found that compression of the thoracic portion of the aorta was associated with increased blood volume and elevation of the pulmonary pressure. Wiggers[37] and Katz and Wiggers[38] in carefully controlled experiments observed normal or but slightly elevated pulmonary pressure. However, moderate increase in the blood content of the pulmonary vessels as present in hypertension does not necessarily indicate increase in pressure, and therefore the above finding does not give any indication as to whether or not in man the pressure in the lesser circulation is elevated.

As observed in a previous study[34] the average *vital capacity* of the lungs in patients with hypertension was lower than the average normal value although their capacity for work was not reduced. So the average vital capacity of patients with normal functional capacity was 1900 c.c. per square meter of body surface instead of the normal 2500

c.c. per square meter of body surface. In view of the fact that the amount of blood in the lungs of patients with normal functional capacity is increased, this increased blood content of the lungs in hypertension may be one of the factors responsible for the reduction of the vital capacity.

F. *The Significance of the Observations Presented on the Problem of the Therapy of Hypertension.* According to the evidence presented, the most significant difference between the circulation of the patients and of the normal subjects is in the resistance offered by the arteriolar system and in the arterial and arteriolar pressure of the greater circulation. Notwithstanding the presence of high arteriolar resistance, the mean velocity of the circulation and the amount of blood flowing through the capillary bed per unit of time, as well as the capillary pressure are normal. Considering that the total circulating blood volume and the pressure in the venous system is normal, because the blood volume of the lungs is increased, the volume of the blood in the arterial and capillary system is smaller than in normal individuals. It is by the aid of increased pressure in the arterial system that the heart reinstates the normal capillary flow and pressure. This reestablishment of normal capillary circulation is achieved with great economy as far as cardiac work and peripheral circulation are concerned. With the exception of the high basal metabolism occasionally observed, we have noted no bodily functions which may be considered, *a priori*, as uneconomical or superfluous. If the high basal metabolism associated with hypertension is due to primary hyperfunction of the thyroid gland and is not secondary to the high blood pressure, then, as has been pointed out, the circulation functions with better economy in these patients than in hyperthyroid patients with normal blood pressure.

As indicated above, there must be a definite relationship between pressure and volume of blood flow corresponding to a given increased peripheral resistance. $R = \frac{P}{V}$. Therefore, if the peripheral resistance could be measured directly, assuming that the normal or slightly subnormal minute volume approximates the optimal for physiological needs, then one could foretell the optimal blood pressure required for an abnormally high resistance. If the heart can not throw out the normal amount of blood, V becomes smaller and, correspondingly, if the resistance is unchanged, P will fall. Under such conditions the blood circulates through the vital organs in such a way that its volume flow and pressure are both less than the optimal, and unless the capillary circulation is able to compensate for the cardiac failure, serious disturbances develop in the function of the body. The onset of circulatory disturbances occurs at different arterial pressure levels for different patients, depending on the degree of increase in the peripheral

resistance. The findings and discussion presented above offer a rational explanation of the weakness, dizziness, choking sensation and other symptoms and signs of incompetent circulation felt by patients with the onset of a decrease from the optimal blood pressure.[39] Unless, therefore, the cardiac output is known, the significance of a fall in blood pressure following therapeutic procedures can not be judged. The administration of therapeutic agents in hypertension should be combined with quantitative measurements of the circulation of patients before and after treatment. Only by such measurements will harm to the patient be averted. Without a corresponding reduction in the peripheral resistance, reduction of the blood pressure should not be an aim in the treatment of hypertension. Because the volume and velocity of blood flow are never above normal in hypertension, the therapeutic efforts should be directed either toward the maintenance of the optimal blood pressure and volume flow for a given abnormally high peripheral resistance, or toward the reduction of the blood pressure through lowering the abnormal resistance. Therapeutic procedures that lower the blood pressure through decreased cardiac output are harmful. In patients in whom the resistance can not be altered (fixed hypertension), and whose pressure is distinctly below optimal, it is in the interest of the patient to reestablish higher arterial pressure, through the improvement of the cardiac function.

Thus there can be no uniform treatment for arterial hypertension. Progress in therapy can come only through study of the circulation of the individual patient. The knowledge gained in this will determine the proper selection of therapeutic measures, the rational application of which rests on logical pharmacological and therapeutic observations.

SUMMARY AND CONCLUSIONS

1. A study is presented of the circulatory mechanism in 30 patients with hypertension.

2. Although the average resistance of the arteriolar system of the greater circulation was twice as great in the patients as in the normal control subjects, the circulating blood volume, the cardiac output per minute, the arm to face velocity of the blood flow, and the mean velocity of the circulation were either normal or slightly below normal.

3. The calculated volume of blood in the lungs in hypertension is increased.

4. The volume content of the arterial and capillary bed of the greater circulation in hypertension is probably reduced.

5. Although the peripheral resistance was increased to twice normal, the estimated work of the left ventricle of the heart in hypertension was only 41 per cent greater than in normal subjects. This work corresponds to an energy consumption of 10.7 per cent of the basal metabolism.

6. Tissue nutrition in the presence of hypertension is accomplished with a distinct economy of the cardiac work and the various functions of the peripheral circulation.

7. In patients with hyperthyroidism and normal blood pressure, the heart rate, the cardiac output and the velocity of blood flow are increased in proportion to the increased basal metabolism; in certain patients with essential hypertension showing clinical evidence of overactivity of the autonomic nervous system, the heart rate, the cardiac output and velocity of blood flow may be within the limits of normal although the basal metabolism is increased.

8. The mechanism of circulation is similar in patients with primary nephritis and secondary hypertension to that in patients with primary hypertension.

9. A satisfactory explanation for the dynamics of the circulation in the patients with hypertension studied is that due to the abnormally accentuated arteriolar resistance, a high arterial and arteriolar pressure is essential to reestablish the normal capillary blood flow and pressure in the vital organs.

10. The measurements and observations do not bear out the hypothesis that loss of the elasticity of the great arteries, or increased cardiac output, or increased circulating blood volume, or hypoventilation and decreased blood content of the lungs is responsible for the presence of hypertension.

11. The relationship between cardiac output, arterial pressure, peripheral resistance and capillary circulation determines the nature of the therapeutic procedures applicable in hypertension.

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THE DISAPPEARANCE OF INTRAVENTRICULAR HEART-BLOCK OCCURRING IN UREMIA FOLLOWING THE INTRAVENOUS INJECTION OF HYPERTONIC GLUCOSE SOLUTION*

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THAT there are alterations in the cardiac muscle in uremia occurring in the course of nephritis is well known. The occurrence of pulsus alternans during this state has been observed.[1] Wood and White[2] studied the electrocardiograms of patients exhibiting symptoms of uremia. They found changes in the form of the T-wave in Lead II, less often abnormal rhythms, and rarely an increase in the auriculoventricular time interval or in the duration of the QRS complexes. They concluded that "in certain cases of uremia and severe nephritis with increased blood nitrogen there is a toxic effect acting in some respects like digitalis on the heart muscle, which may produce abnormal electrocardiograms."

Recently a patient under our care developed intraventricular heart-block while in the state of uremia. Shortly after the intravenous injection of hypertonic solution of glucose, the electrocardiogram changed, intraventricular heart-block disappeared. We have been unable to find in the literature the record of such an occurrence. It is for this reason that we wish to make report of this observation.

Although the rôle of sugar in the metabolism of cardiac muscle has been the subject of many investigations, the effect of the injection of glucose in abnormal cardiac rhythms such as occur in the clinic and may be recorded electrocardiographically has not been studied. That there is consumption of dextrose in the circulating fluid by the isolated and perfused mammalian heart was first shown by Johannes Müller[3]; the steps in the process of its utilization, however, are not at present definitely known.

CASE HISTORY

The patient, a male seventeen years old, was admitted to the hospital on November 29, 1928, complaining of weakness, dyspnea and swelling of the ankles. The patient was examined for life insurance five months previously and was told that albumin and red blood cells were present in the urine. He felt well, however, and continued working for one month when swelling of the ankles was observed. After four and one-half weeks in the hospital he became free of edema. One week later edema of the feet recurred. One month later he entered another hospital, having

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been free of symptoms although edema was still present. Here a diet high in protein content was given for one month. While in the second hospital and three weeks before admission to this hospital, he was suddenly seized with a chill and fainted. After this experience, he suffered from frequent attacks of fainting. He was occasionally nauseated and was short of breath for one month before admission to this hospital.

The patient's general health had always been good. He had an attack of measles during childhood from which he made a prompt recovery. He had suffered from colds and sore throats infrequently. Tonsillectomy had been performed twelve years before and a submucous resection of the nasal septum seven months before admission to hospital. There had been no cardiorespiratory, gastrointestinal or genitourinary symptoms until the onset of the present illness. His family history was unimportant.

On physical examination, the patient was a well-developed boy of seventeen years. There was pallor of the skin and mucous membranes. The pupils were regular and equal; they reacted to light and in accommodation. The fundi were normal on ophthalmoscopic examination. There was no tenderness over the sinuses. The ears were normal. The nasal septum was deflected to the right. The teeth and gums were in good condition. The tonsils appeared as small nodules buried in scar tissue. The breath was foul. The neck was normal. The lungs were normal to percussion and auscultation. The point of maximal impulse of the heart was felt in the fourth interspace, 6.5 cm. from the midsternal line. The rhythm was regular. A systolic murmur was heard along the left sternal margin. A diastolic murmur was not heard. The radial vessels were soft. The pulses were equal at the two wrists. The systolic blood pressure measured 166 mm. of mercury, the diastolic 86 mm. The abdomen was negative. The deep reflexes were present and active. There was pitting edema of the ankles.

On admission to hospital a twelve-hour concentrated specimen of urine contained 60,000,000 red blood cells, 10,000,000 white blood cells and epithelial cells, and 4,920,000 casts, 95 per cent of which were hyaline in type (Addis[4]).

The count of the red cells in the blood was 3,400,000 and that of the white cells 23,200, 84 per cent of which were polymorphonuclear, 10 per cent lymphocytes and 6 per cent transitionals. The oxygen capacity of the blood was 12.5 volumes per cent, equivalent to 68 per cent hemoglobin. The nonprotein nitrogen of the blood was 43 mg. per cent and the blood urea nitrogen 29 mg. per cent. The plasma proteins were reduced, the albumin to 1.6 per cent and the globulin to 2 per cent. The renal function as estimated by urea clearance was 27 per cent of normal (Möller, McIntosh and Van Slyke[5]).

In a two-meter x-ray photograph of the chest the heart did not appear to be enlarged.

The diagnosis according to the Addis classification[6] was hemorrhagic Bright's disease—active stage.

Course in Hospital

During the first five months the patient was under observation, the renal function, blood urea nitrogen, blood pressure and hemoglobin continued at the same level as on admission (Fig. 1). There was, however, a slight rise in the protein content of the blood plasma. During the fifth month tonsillectomy and adenoidectomy were performed to eliminate foci of infection. For several days after operation, oozing of blood from the nasopharynx occurred. Two weeks later the patient became anuric for three days. Catheterization at the end of that time yielded only 420 c.c. of urine. There were signs of uremia; vomiting started and became more frequent; the blood urea nitrogen rose to 114 mg. per cent (Fig. 1). Five days later, vomiting occurred several times each day; the patient became dehydrated and hypodermoclyses were given daily. On the morning of June 9,

1929; examination of the heart revealed the presence of gallop rhythm, best heard along the left border of the sternum. The rhythm was regular; a systolic murmur previously noted was still heard; the pulse was regular but weak. An electrocardiogram was taken immediately after examination. Intraventricular heart-block was present (Fig. 2, before injection of glucose intravenously). Since it had been observed on a previous occasion in another patient suffering from uremia, that which was thought clinically to be heart-block with syncope (Stokes-Adams syndrome) disappeared following the administration of hypertonic solution of glucose intravenously, 50 c.c. of a 50 per cent solution of glucose were given intravenously.

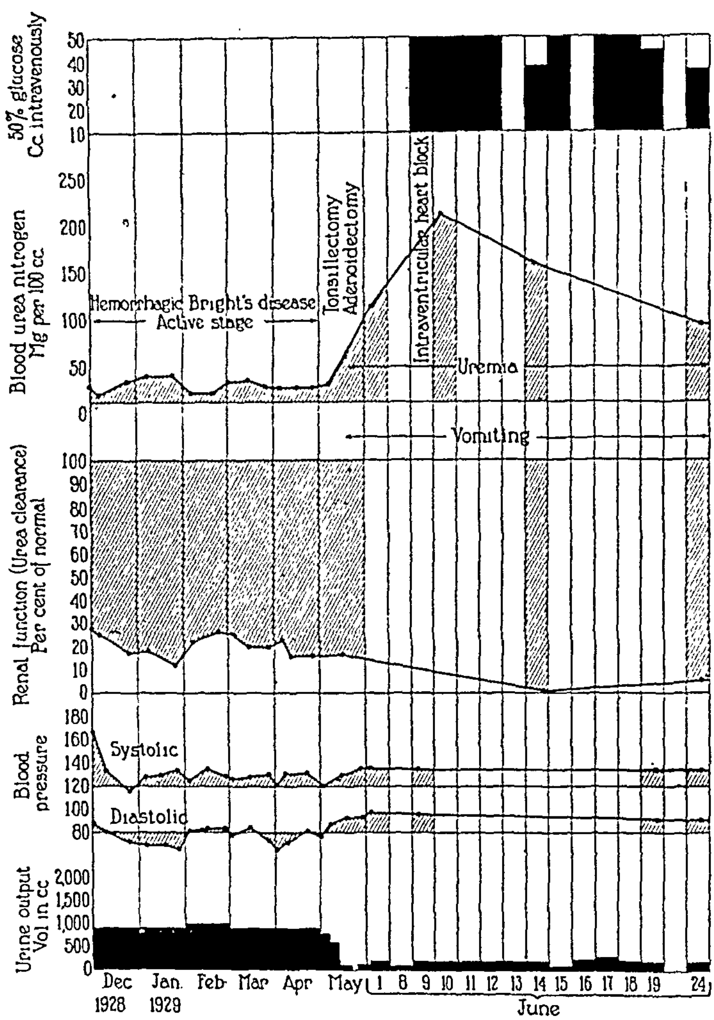

Fig. 1.—In this figure the clinical course of the patient is shown graphically. The output of urine, the blood pressure, the renal function and the blood urea nitrogen are recorded. Cross hatching indicates per cent deviation from normal, solid black represents amount in cubic centimeters. The day on which intraventricular heart-block occurred (June 9) is indicated.

There was an immediate change in the patient's condition as soon as the injection was begun: the gallop rhythm disappeared, the radial pulse became more forceful, and the patient volunteered the information that he felt very much better. Within one half hour a second electrocardiogram was taken; intraventricular heart-block had disappeared (Fig. 2, see description of electrocardiograms). Improvement was, however, temporary; the patient became drowsy and vomiting set in a few hours later. Gallop rhythm, however, did not recur, nor did intraventricular heart-block.

The next day, the blood urea nitrogen was 216 mg. per cent. Hypertonic glucose

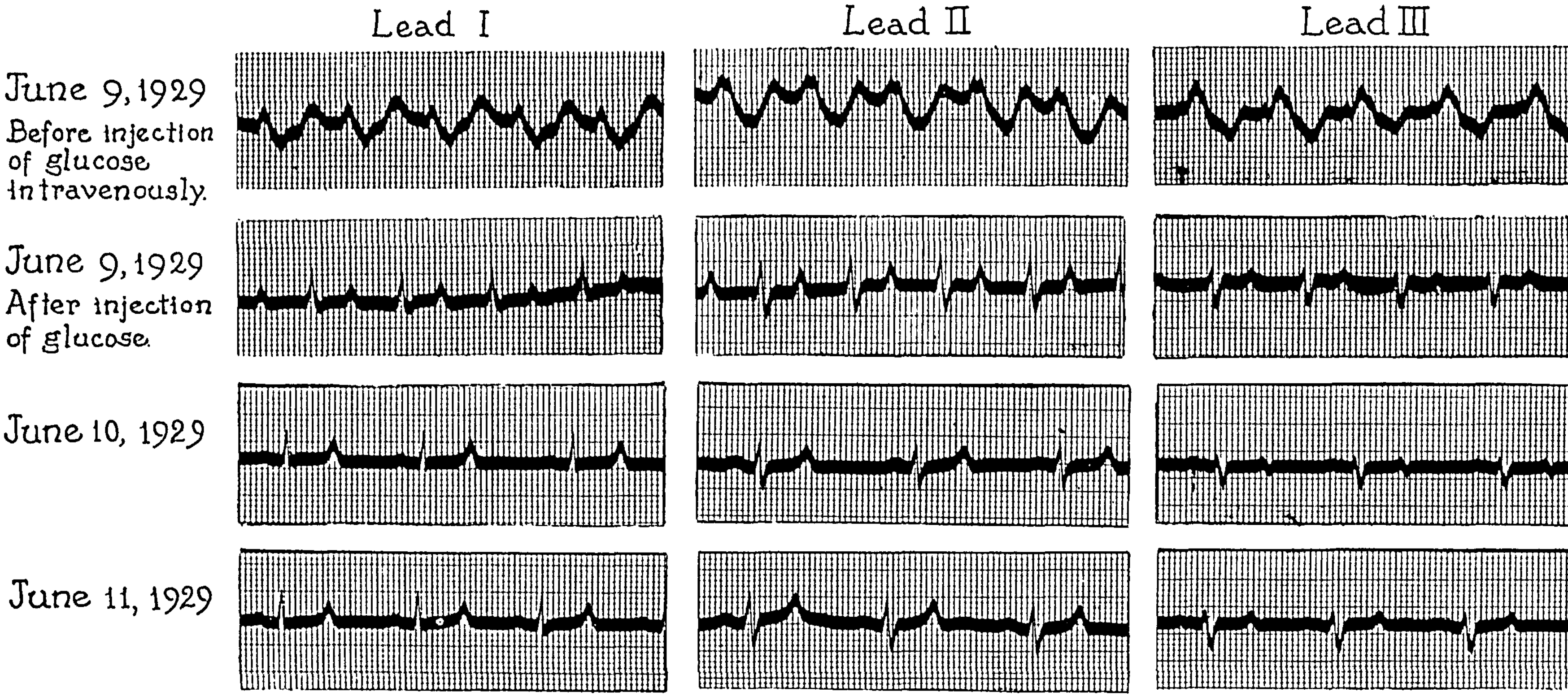

Fig. 2.—In this figure are presented the electrocardiograms derived from the patient. For description see text. The three standard leads of the electrocardiogram are shown. The standardization was such that a deflection of 1 cm. of the string was equivalent to 1 millivolt. Divisions of the ordinates equal 10^{-4} volts. Divisions of the abscissae equal 0.04 of a second. The electrocardiograms are reduced to five eighths of their natural size.

solution was administered daily on the next three days (Fig. 1). Temporary improvement occurred after each injection. Vomiting continued, however. A test of renal function made five days after the first injection of glucose showed that it was only 2 per cent of normal; blood urea nitrogen was 165 mg. per cent. During the next week glucose was given on five days, followed by a period of four days on which none was given. On June 24, the last day the patient was given glucose, the blood urea nitrogen was 96 mg. per cent; there was slight rise in renal function (Fig. 1), and the clinical symptoms of uremia were less marked. The patient gradually became worse, however, and died nine days later. Before death occurred the blood urea nitrogen increased to 127 mg. per cent and the urea clearance fell to 1.7 per cent of normal.

Electrocardiograms

The electrocardiograms taken immediately before injection of 50 c.c. of 50 per cent solution of glucose showed auriculoventricular rhythm (best seen in Lead III, Fig. 2). The prolonged QRS interval (0.16 of a second) together with splitting of the QRS waves gave indication of marked functional or anatomical alterations of the heart muscle. The slightly negative phase of the T-waves in Lead I was followed by a positive swing of greater voltage, while the deep negative phase of the T-waves in Leads II and III was followed by a positive swing. In short, *intraventricular heart-block was present.* The ventricular rate was 100 per minute. One half hour after the intravenous injection of glucose the electrocardiogram had changed; auriculoventricular rhythm was still present, the ventricular rate being 100 per minute. *Intraventricular heart-block was, however, no longer present.* The QRS time had decreased to the extent that it was now within normal limits. There was left axis deviation. It may be recalled that coincident with these changes the radial pulse improved in force, and there was marked subjective and objective improvement. The next day (June 10, twenty-four hours later) the rhythm was normal and the ventricular rate slower (70 per minute). The conduction time in Lead II was 0.16 to 0.17 of a second. The T-waves in Lead III were diphasic. There was still slight splitting of the QRS complexes, the QRS time, however, was within normal limits. The next day the rhythm remained normal and the P-R interval was 0.2 of a second. The only change to be observed in the form of the curves was that the T-waves in Lead III, which had been diphasic, were now upright and of greater voltage. From that time the electrocardiograms remained essentially unchanged. There was no recurrence of intraventricular heart-block.

DISCUSSION

The cause of the changes which occur in electrocardiograms in the course of uremia can be at present only a matter of conjecture. The abnormalities which have been found have been attributed to nitrogen retention. Wood and White[2] found, however, that no correlation existed between the degree of nitrogen retention and the tendency to exhibit electrocardiographic changes. From observations made on the electrocardiograms of patients, Robinson[7] has attributed transient intraventricular heart-block to a state of poor nutrition of heart muscle. That the changes are more likely to be of a toxic nature (functional changes) than due to anatomical lesions is clearly demonstrated in the case of our patient, by the rapidity of the disappearance of the abnormality. Several days before the onset of uremia there was anuria and associated with this a rise in blood urea nitrogen (from 35 mg.

per cent to a level of 216 mg. per cent). It was then, when the urea clearance was only 2.4 per cent of normal, that his electrocardiogram showed the presence of intraventricular heart-block. One-half hour after the injection of 50 c.c. of 50 per cent solution of glucose intravenously intraventricular heart-block disappeared, and the patient's general condition began to improve. Other observers (Budingen,[8] Isaac[9]) who have used hypertonic glucose solutions intravenously in a variety of conditions have observed an increase in force and volume of the radial pulse. This effect has been attributed by them to two factors: in the first place, to the improved nourishment of the heart muscle; and in the second place, to an osmotic pressure effect due to the fact that hypertonic glucose solutions draw water from edematous heart muscle. Their argument presupposes, of course, that there is edema of heart muscle.

A basis for the use of glucose solutions in states in which it is believed the muscle is undernourished is found in a long series of experiments. It may be recalled that Johannes Müller[3] first demonstrated that there is consumption of dextrose in the circulating fluid by the isolated and perfused mammalian heart; Stewart[10] made a similar observation in regard to the artificially perfused human heart. Locke and Rosenheim[11] showed that there is a definite relation between the amount of sugar consumed and the length of time during which the heart is kept beating. In perfusing hearts of rabbits Claes[12] demonstrated that the presence of an increased amount of glucose in the perfusion fluid is very favorable for the work of the heart and that the excitatory action of adrenalin is prolonged by it. The effect of cardiac rate on the utilization of sugar has also been studied. Patterson and Starling[13] found that an acceleration of the rate due to adrenalin causes increase in sugar consumption. And if insulin is added to the blood of the heart-lung preparation, Plattner[14] found that the rate of disappearance of blood sugar did not increase so long as the rate was not accelerated; if it did, the disappearance of sugar was found to increase in the same ratio after the addition of insulin to the perfusion fluid. Hepburn and Latchford[15] showed that the addition of insulin to the perfusion fluid accelerated the removal of dextrose therefrom by the isolated mammalian heart. Burn and Dale[16] have shown that the extra sugar does not disappear by combustion.

The energy requirements of the heart for a given stroke volume increase with an increase in the diastolic volume, so that the efficiency decreases (Starling and Visscher[17]). In the heart-lung preparation the heart slowly and continually dilates; although, according to Starling, under physiological conditions it always works at the smallest possible volume and with a maximum efficiency; this dilatation can be abolished by the addition of insulin (Visscher and Müller[18]). Bayliss, Müller and Starling[19] have shown that the heart volume can be re-

duced by the addition of insulin to the perfusate, but the effect is transitory unless glucose is also given either before or after insulin, when it lasts an hour or more. Neither insulin nor sugar has any action on hearts already working efficiently. The volume of the heart is reduced by adding glucose alone as well as insulin alone, and by the same terms its efficiency is increased. In the absence of insulin enormous concentrations of glucose are needed in the blood in order to permit the heart to function properly, and subsequent addition of insulin causes a rapid disappearance of much of this glucose. The sugar does not, as has already been suggested, disappear by combustion. The results are explained by assuming a reaction between free glucose and a substance which they call "stored glucose" or "glucose complex," in the elaboration of which insulin plays a part. Edmunds and Cooper[20] have observed in dogs a rise in blood pressure following the intravenous injection of glucose in the circulatory failure which follows the injection of diphtheria toxin.

It appears then both from experiments in the laboratory and from observations made in the clinic that glucose has an influence upon the behavior of cardiac muscle. The effect may be stated in a general way to favor the mechanical capability of the muscle. From our experience in this case it appears that glucose has a further influence, for as a result of giving it the propagation of the excitatory wave through the ventricular muscle was improved. The muscle cells, in which before there was a delay in the propagation of the excitatory process, were altered in such a fashion that the excitatory wave now passed through the muscle in a time which was within normal limits.

It is not possible to state accurately by what mechanism the injection of glucose induced the changes in the electrocardiograms which were observed; whether by improved nutrition of the heart muscle or by an osmotic pressure effect, by a combination of the two, or by some other factors. That there was an association between the occurrence of intraventricular heart-block in uremia and its disappearance in this patient following the injection of glucose is apparent.

SUMMARY

Report has been made of the disappearance of intraventricular heart-block occurring in the course of uremia following the intravenous injection of hypertonic solution of glucose.

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PAROXYSMAL TACHYCARDIA WITH MYOCARDIAL LESIONS*

A Case Report

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Many observations have been made upon paroxysmal tachycardia in the past few years, but most of these studies deal largely or entirely with electrocardiographic aspects of this condition. The number of cases in which pathological studies have been reported is comparatively small.

In 1926 we[1] reported a case of paroxysmal tachycardia, probably of ventricular origin, in which the heart showed numerous foci of myocarditis, obviously the result of infection. We have recently had the opportunity of studying a patient suffering from paroxysmal tachycardia of auricular origin, who died during the attack and on whom a necropsy was obtained. The history of this patient is as follows:

Mrs. G. N., aged thirty-four years, was admitted to the Bell Memorial Hospital complaining of rapid heart, nausea, and swelling of the abdomen.

Family History: Essentially negative.

Past History: The patient was married and had three children. There is no history of miscarriages or difficulty in labors. The patient has had attacks of rapid beating of the heart, coming on suddenly and disappearing equally suddenly three or four time a year since she was thirteen years old. The duration of these attacks has varied from a few minutes to two days. During the past six months, she has had two attacks, each of which lasted only one hour. The patient has suffered for years from numerous attacks of tonsillitis and her tonsils were removed one year ago and found to be badly infected.

Present Illness: The present illness began suddenly two weeks before admission to the hospital. This attack resembled the previous attacks the patient had had, but has continued much longer than any previous attack. The past few days the patient has been blue and very short of breath.

On physical examination the patient had a strikingly distressed and anxious look, the precordium was heaving and it was obvious that the heart was beating at a rapid rate. The pulse was so rapid that it could not be counted at the wrist. The patient's blood pressure was 90 mm. systolic and 60 mm. diastolic; respiration was rapid (40 per minute); and on auscultation there were numerous fine, moist râles heard throughout the chest.

The liver was palpable 6 cm. below the costal margin in the right mammillary line; the abdomen was distended, and there was a marked fluid wave. Both legs were edematous and pitted on pressure. The urine showed a trace of albumin, the blood examination showed: R.B.C. 4,000,000; W.B.C. 14,200; hemoglobin 70 per cent. The roentgenographic findings showed an increase in the size of the heart and evidences of chronic pulmonary tuberculosis at a hilum of the lung. The electrocardiograph showed the heart rate to be 240 per minute.

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The clinical picture was that of a paroxysmal tachycardia which had continued such a length of time as to produce a marked myocardial insufficiency. The electrocardiogram taken of this patient (Fig. 1) shows a tachycardia, probably of auricular origin. The patient was given strophanthin intravenously, combined with luminal and morphine, and she also received several doses of quinidine. Following the use of quinidine, there seemed to be a progressive slowing in the heart rate, and on December 31 the pulse rate was diminished to 180; on January 1 the pulse rate was down to 164; on January 3 the pulse rate was 160; on January 4 in the

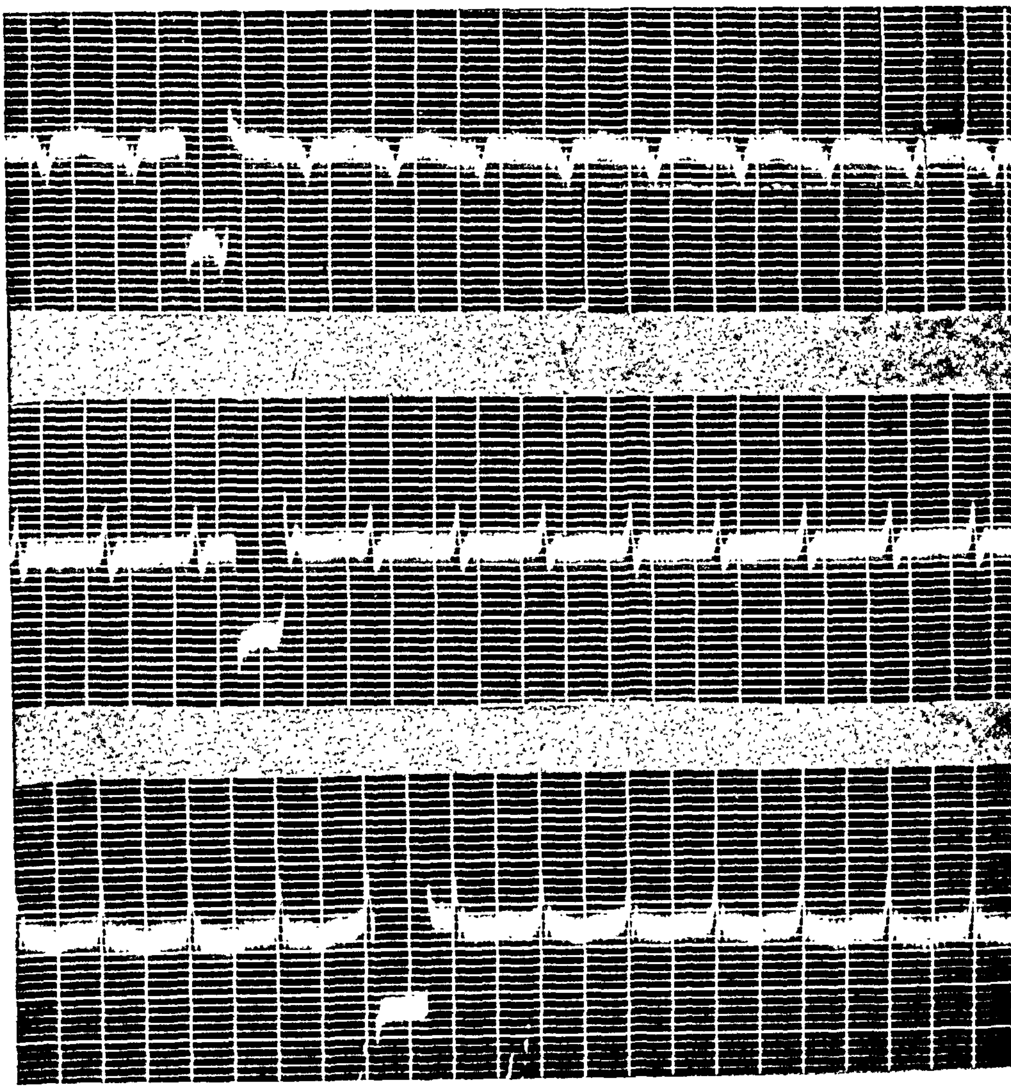

Fig. 1.—Electrocardiogram of heart during tachycardia.

morning, the rate was 148, falling to 100 in the afternoon. The morning of January 5 the pulse rate again rose to 151 and, shortly after, the patient became very cyanotic and died suddenly. A few minutes before death she seemed apparently comfortable, smiled, talked, and expressed herself as feeling very much better.

Autopsy: The autopsy was performed the same day. The anatomical diagnosis was: acute and chronic myocarditis (focal); acute mural endocarditis with organizing mural thrombosis; chronic pericarditis with subepicardial hemorrhages; fragmentation and segmentation of the myocardium; hypertrophy and dilatation of the heart; infarction of the lungs; pulmonary thrombosis; general anasarca;

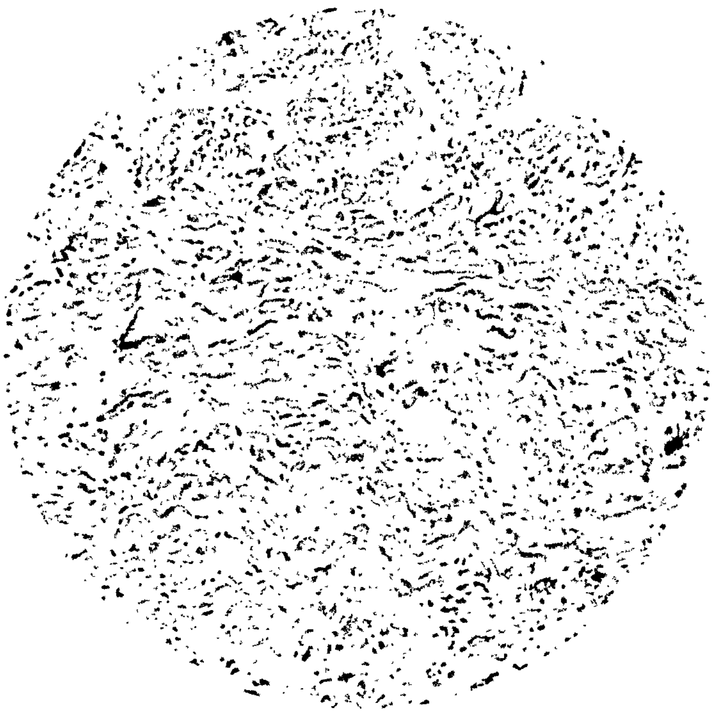

Fig. 2.—Section of myocardium in ventricle showing fibrosis, fragmentation, and necrosis of muscle cells. (Magnification ×200.)

Fig. 3.—Mural endocarditis showing edge of thrombus. (Magnification ×175.)

toxic nephrosis; acute and chronic pancreatitis; chronic passive congestion of the liver, lungs, and kidneys; fatty degeneration of the kidneys; partly healed caseous tubercle of the lungs; chronic adhesive pleurisy; atelectasis, chronic bronchitis, and chronic pneumonitis.

The most interesting necropsy findings were in the heart. The pericardial sac was distended with fluid. The surfaces were smooth, moist, and glistening. The heart weighed 345 grams and measured 12 by 10 by 8 cm. and was normal in shape. It was firm, reddish-brown, somewhat dilated, and the chambers were filled with fluid blood. The foramen ovale was closed. The pericardial surfaces were smooth, moist, and glistening. Thrombotic masses were adherent to the auricular wall, particularly on the right side, but elsewhere the mural and valvular endocardium was normal. The subepicardial fat was scanty, but in the auricles it showed a number of small petechial hemorrhages. The myocardium of the right ventricle

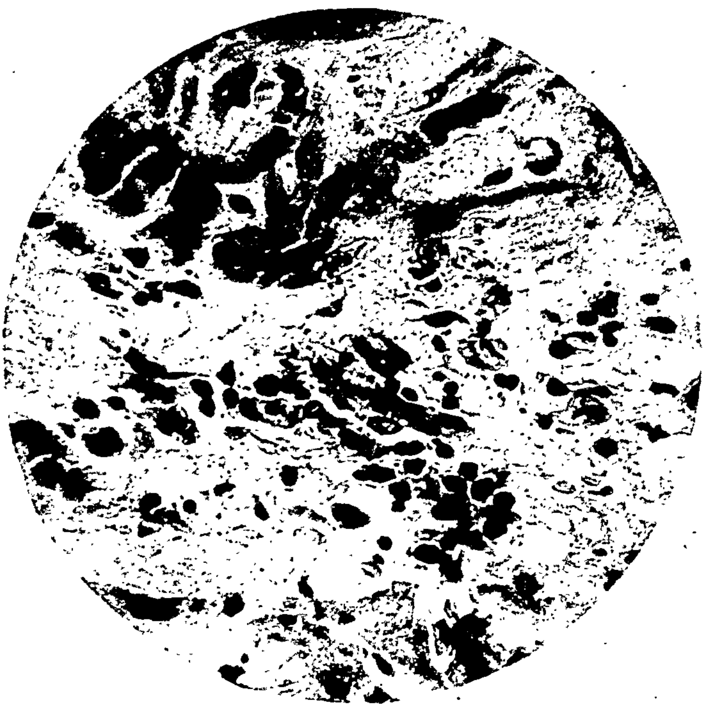

Fig. 4.—Perivascular inflammatory reaction in myocardium. (Magnification ×400.)

varied from 4 to 7 mm. in thickness and that of the left, from 16 to 20 mm. The chordae tendineae and papillary muscles showed nothing abnormal. The circumferences of the valve rings were as follows: tricuspid 13, mitral 11, pulmonary 8.5, and aortic 6 cm. The coronary arteries showed nothing abnormal.

On microscopic examination the pericardium was thickened. It showed here and there foci of lymphoid cells, especially about some of the blood vessels. In some places there was congestion of the vessels associated with focal hemorrhages and lymphoid cell infiltration. The changes in the pericardium and in the musculature of the auricles were more striking than those in the ventricles. The endocardium was in places slightly thickened, and showed some infiltration of leucocytes. One area showed both polynuclear and mononuclear leucocytes extending throughout the endocardium, and adjacent to this was a typical early organizing thrombus. The endocardial lesions here also were limited to the auricles. The muscle fibers of the auricles showed marked atrophy with degeneration and some replacement by fibrous

tissue. In some microscopic fields there was much fragmentation and segmentation and necrosis. The cross striations of the muscle fibers were often obscure; and many fibers showed marked vacuolar and granular degeneration with pyknotic, irregular, and hyperchromatic nuclei. In some foci the stroma was considerably increased in amount, particularly in the neighborhood of the blood vessels. Foci of leucocytes were fairly common, which showed large mononuclear cells, often with eosinophilic cytoplasm. Occasionally polynuclear leucocytes were seen, usually in some of the congested blood vessels. Although these degenerative changes were also seen in the ventricle, most of the focal inflammatory changes were seen in the auricle.

A section of the heart muscle stained with scharlach R showed some fat droplets in the muscle fibers, particularly near the nuclei. Some of these droplets were lipochromes.

The degenerative and inflammatory foci were more marked and numerous in the auricle than in the ventricle. The inflammatory changes were not only acute but also chronic, there being rather extensive diffuse fibrosis particularly in the sections of the auricle.

This patient who suffered from paroxysmal tachycardia showed at autopsy an acute and chronic myocarditis. This myocarditis was very obviously infectious, and the patient's infected tonsils, which were removed approximately one year before the onset of this attack, may have been the portal of entry for the infection.

It is interesting that this patient's attacks at first had a very sudden onset and a sudden termination, and clinically belonged definitely in the group described by Bouveret, who insisted upon this criterion for diagnosis. In this last attack, however, the tachycardia did not cease suddenly, but gradually, the patient's pulse coming down to normal over a period of four days. The duration of this attack was unusually long, the patient having had the condition two weeks before admission and being under observation ten days in the hospital—twenty-four days in all.

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SO-CALLED INTERPOLATION OF EXTRASYSTOLES DURING IDIO-VENTRICULAR RHYTHM*

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THE term interpolation in clinical electrocardiography is used to denote interposition in a series. An interpolated ventricular extrasystole is interposed between two beats of the sequence initiated from the pacemaker. It differs in effect from the ordinary ventricular extrasystole in that it fails to block completely, although it may delay the transmission of the next expected beat of the sequence.

Interpolation occurs readily when the combination of slow heart rate and highly premature beats is present. These circumstances permit time for recovery of the junctional tissues after block of the retrograde impulse of the premature beat before the next expected impulse from the pacemaker arrives. If, however, idio-ventricular rhythm is present the state of affairs becomes very unfavorable for interpolation because of the comparative accessibility of the pacemaker to the influence of the excitatory wave of the premature beat. Nevertheless, interpolation is theoretically possible and should occur if the idio-ventricular pacemaker is protected from the premature beat and the conducting tissues between the pacemaker and the ventricles recover rapidly enough to transmit the next expected excitatory wave.

Weiser[1] has reported a case of transient complete heart-block due to digitalis, in which ventricular extrasystoles caused only very slight disturbance in the fundamental idio-ventricular rhythm. He interpreted his curves as showing interpolation of ventricular extrasystoles and referred to tracings previously published by Fahrenkamp[2] and Singer and Winterberg[3] which he believed also exhibited interpolation. Singer and Winterberg's tracing is susceptible of an entirely different interpretation which need not be considered here. A characteristic of Fahrenkamp's as well as Weiser's curves was the fact that the cycles containing extrasystoles were slightly longer than uninterrupted cycles. This finding is somewhat difficult to harmonize with the interpretation given, but Weiser assumed that it was due to temporary delay in responsiveness of ventricular muscle to excitation caused by incomplete recovery from the preceding extrasystole. Although Weiser does not so state, the delay in his case would have to occur in the auriculo-ventricular bundle because of similarity of ventricular complexes. However, if the disturbance involved the rate of trans-

*From the Robinette Foundation, Medical Clinic, Hospital of the University of Pennsylvania.

mission rather than the rhythmic discharge, one would expect the delay in the cycle containing the extrasystole to be compensated for in the next succeeding cycle or cycles. This evidence would be necessary in Weiser's case to establish clearly his contention that the extrasystoles are actually interpolated and not due to interference with the centre. Unfortunately, the tracings do not furnish this data but it is stated that cycles containing extrasystoles have a duration of 1.55 second and other cycles 1.50 second.

We have obtained tracings in one case of complete heart-block with ventricular extrasystoles in which the cycle containing extrasystoles are 0.06 to 0.07 second longer than other cycles, (Figure 1) a time relation practically identical with that of Weiser's case. In our case the delay was not compensated for in the succeeding cycle. It is therefore necessary to conclude that the extrasystoles caused a disturbance in the rhythmic discharge of excitations rather than in their transmission.

If one speculates as to the mechanism concerned in our case, two possibilities present themselves. First, the premature excitation of an extrasystole may reach the active idio-ventricular centre and abolish the impulse building there but fail to reach another centre capable of discharging impulses at a slightly slower rate. Thus, after an extrasystole, such a centre which had been protected from the premature disturbance would be given an opportunity to discharge an excitation. In both Weiser's and Fahrenkamp's cases this view finds support in that the presence of slight changes in the QRS complexes following extrasystoles suggest that the excitation had spread through a slightly different pathway. This finding is especially noteworthy in Fahrenkamp's case which showed a succession of cycles, each containing what Weiser interpreted as an interpolated extrasystole. Alternate differences in QRS complexes were present as though two idio-ventricular centres were alternating in activity. McMillan and I[1] have pointed out the possibility that differences in ventricular complexes may depend upon differences in the lengths of pathways to the main branches of the bundle. Thus a centre just above the bifurcation nearer the right main branch might be expected to excite responses with ventricular complexes slightly different from those of a centre nearer the left main branch.

The second possibility assumes that the regularly functioning idioventricular centre is actually protected from the premature impulse but that the extrasystole causes a reflex nervous disturbance which acts on the centre, delaying the discharge of the next expected excitation. This assumption finds support in the fact that an extrasystole not infrequently disturbs the next few beats of sinus rhythm; an effect doubtless due to reflex nervous influence. Furthermore, there is excel-

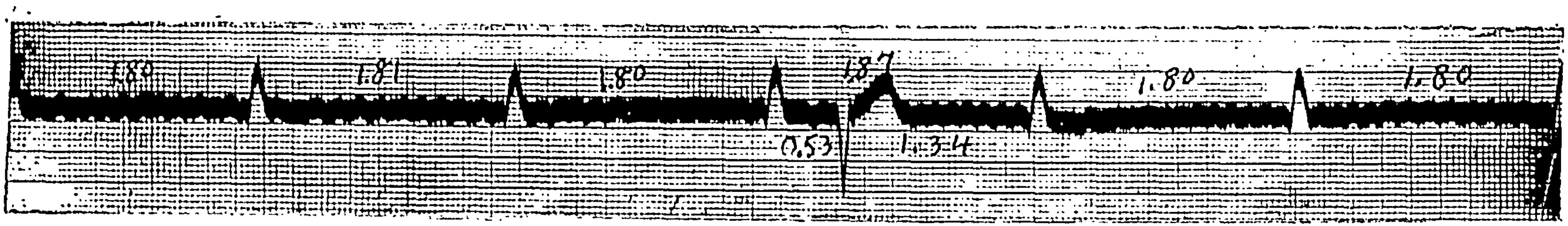

Fig. 1.—Auricular fibrillation and complete heart-block. The ventricular rhythm was remarkably constant except that cycles containing extrasystoles were 0.06-0.07 second longer than others. Exertion and atropin (gr. 1/100 hypodermically) had no effect on the idio-ventricular rate. Tracing made three weeks later was identical except that no extrasystoles were recorded.

lent evidence that both the vagus and sympathetic nerves are sometimes capable of exerting effects on idio-ventricular centers below the point of complete block.[5]

Neither of the above proposed mechanisms, strictly speaking, would justify designating the extrasystoles as interpolated. The term should not be applied in the present state of our knowledge, to extrasystoles during idio-ventricular rhythm unless the dominant rhythm were to remain undisturbed or evidence could be furnished that delay in the beat after an extrasystole is due to prolongation of conduction time from the pacemaker to the ventricles.

The clinical significance of these unusually short pauses after extrasystoles does not depend on whether or not the extrasystoles are interpolated but on the fact that the short pauses may occur during complete heart-block. Their presence therefore should not lead to an erroneous diagnosis of incomplete block.

SUMMARY

An electrocardiogram obtained from a patient with complete heart-block and what might be regarded as interpolated extrasystoles is presented. The mechanism and the possibility of this being true interpolation are discussed.

It is concluded that, thus far, there has been no proof of the occurrence of interpolated beats during idio-ventricular rhythm.

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COMPLETE HEART-BLOCK ASSOCIATED WITH RAPID VENTRICULAR RATE. REPORT OF TWO CASES*

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COMPLETE heart-block is usually associated with ventricular bradycardia. We have recently observed two cases of complete A-V dissociation in which the ventricular rates were rapid, approximately 90 per minute. The association of relative ventricular tachycardia with complete heart-block in cases of auricular sinus rhythm is rare. Lewis[1] makes no mention of it, although he does discuss rapid ventricular rates with complete block in cases of auricular fibrillation. In a review of the literature we have found only six cases resembling the two we are reporting. Luten[2] records four cases of complete A-V dissociation with ventricular rates over 90 in patients who were getting massive doses of digitalis. Carr and Reddick[3] report two cases, one with a ventricular rate of 71 occurring during the acute stage of rheumatic fever in a patient who received 30 c.c. of the tincture of digitalis, and another with a ventricular rate of 83 in a patient who did not receive any digitalis. Dr. William A. Brams has been kind enough to show us an electrocardiographic tracing of a case similar to ours but whose clinical record is unknown. A number of instances are recorded in which the rapid ventricular rate occurring in complete heart-block resulted from ectopic ventricular beats or from two coexisting alternating foci in the ventricles, but the seven cases mentioned and our two are the only ones we can find in which the hyperirritability of the ventricles is manifested by the existence of a single ventricular focus. This focus in each of our cases appears to have been located in or near the A-V node.

REPORT OF CASES

CASE 1.—L. R., male, aged fifty-five years, was admitted to the medical service of Dr. Walter W. Hamburger on February 25, 1929, because of cough, expectoration, dyspnea and edema which had progressively increased over a period of four months. For three months he had been complaining of some left-sided chest pain. Some dyspnea had been present on exertion for the previous two years. The past history was negative except for a cystotomy three years previously for a vesical calculus.

At the time of admission the patient appeared acutely ill; was orthopneic, moderately cyanotic, respirations were Cheyne-Stokes in character, and there was a distinct uriniferous odor to the breath. The mentality was not clear, and the speech was rambling in character. The heart on percussion was enlarged to the left

*From the Medical Services of the Michael Reese Hospital, Chicago.

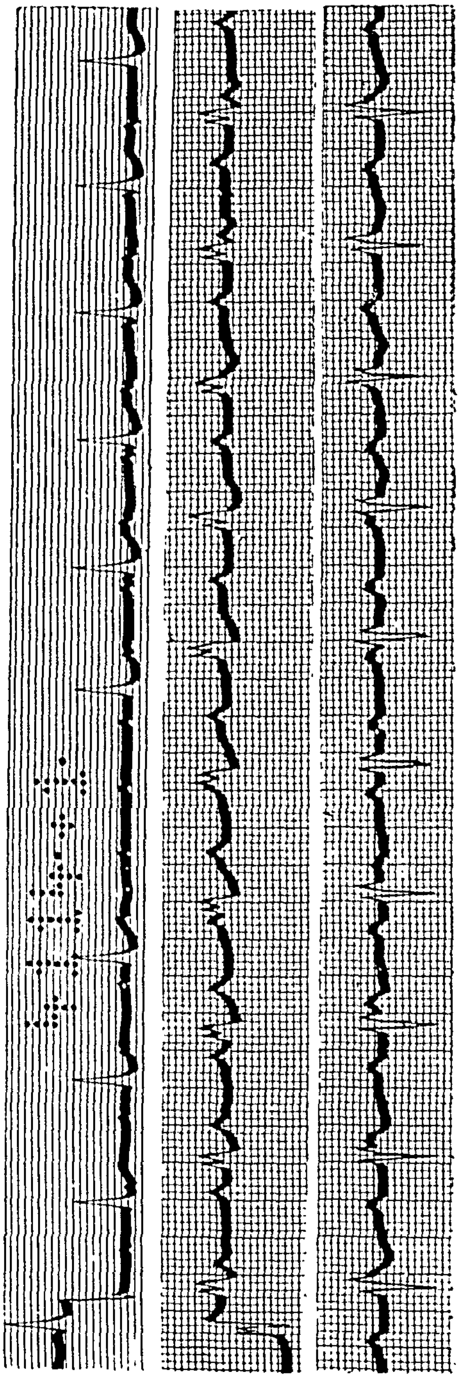

Fig. 1.—Case 1. March 5, 1929. Complete A-V dissociation. The ventricles are responding to a focus in the bundle of His at a rate which varies from 83 to 88 per minute. The auricular rate is approximately 150 per minute. In Lead I, the fourth ventricular cycle is followed by a complete dropping out of the expected ventricular complex. Left axis deviation.

and right, the borders measuring 11 cm. and 4.5 cm. respectively. The rate was rapid. No murmurs were heard. Marked arteriosclerosis was present. Signs of considerable fluid in the right pleural cavity were present, and there were numerous coarse râles in the lower left lung. The liver was enlarged and tender, extending three fingerbreadths below the costal margin. Dullness in the flanks and a fluid wave were elicited in the abdomen. There was marked edema of the legs. The temperature on admission was 100° F., pulse 96, respirations 24. The white blood count was 10,500 with 72 per cent polymorphonuclear cells. The urine contained ++ albumin but no cells or casts. Blood pressure was 144/90 mm. The Wassermann test was negative. The diagnosis on admission included arteriosclerotic heart disease with congestive failure, arteriosclerotic nephritis and uremia.

On February 27, the nonprotein nitrogen of the blood was 62 and creatinin 1.6 mg. per 100 c.c. of blood. Tincture of digitalis, ♏ xxx 4 times daily, was ordered. The general condition remained about the same for three days, following which

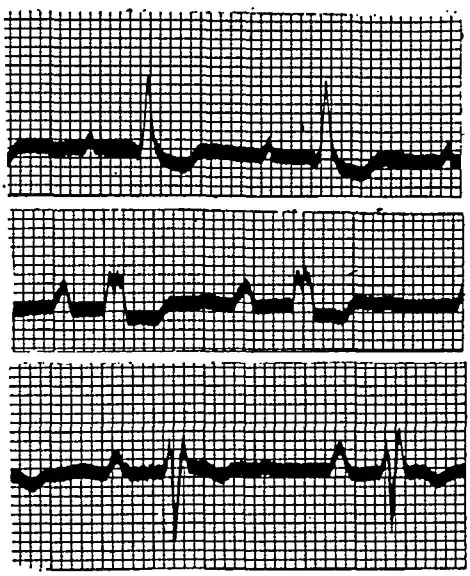

Fig. 2.—Case 1. March 12, 1929. Return to sinus rhythm. P-R interval varies from 0.2 to 0.24 second. The prolongation of the P-R interval is probably due to residual effects of digitalis. Evidences of generalized myocardial damage are present. Left axis deviation.

there was gradual disappearance of the fluid. By March 3, the patient felt greatly improved. Digitalis was continued in the same dosage until March 6 when the patient vomited. This was the first sign of overdigitalization. Digitalis was stopped. The following day the electrocardiogram, which had been taken on March 5, was returned revealing a complete heart-block with a relatively rapid ventricular rate (Fig. 1). On March 12, another electrocardiogram showed that the A-V dissociation had disappeared but that the P-R interval was increased from 0.2 to 0.24 second (Fig. 2). On March 28, the P-R interval had diminished to 0.16 second. On March 18, the nonprotein nitrogen was 39 and creatinin 1.3. Aside from an attack of what was thought to be a right-sided renal colic, the rest of the patient's stay at the hospital was uneventful, and he was discharged March 30 without digitalis. When last seen, April 20, 1929, he was slightly dyspneic. The heart rate was 96. There were no murmurs heard. The lungs were clear, the liver was detected one fingerbreadth below the costal margin, and there was slight edema of the legs.

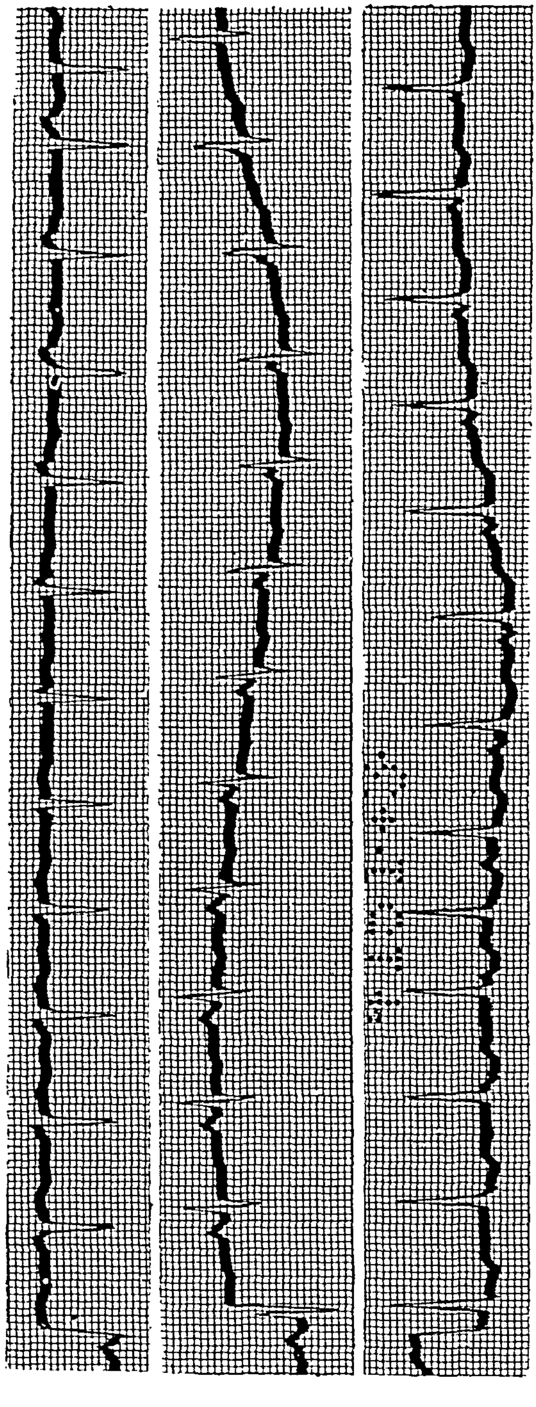

Fig. 3.—Case 2. March 19, 1929. *Complete A-V dissociation.* The ventricular focus lies in the bundle of His and has a rate of 96 per minute. In Lead III there are two ventricular cycles equal to each other but having a duration which corresponds to a rate of 130 per minute. Right axis deviation.

Case 2.—Mrs. J. M., a forty-four-year-old widow, a silk worker, was admitted to the medical service of Dr. Sidney Strauss, March 15, 1929, complaining of dyspnea on exertion and weakness of four years' duration, cough, orthopnea and pain in the chest for two weeks. She gave a history of heart trouble for fifteen years, but no rheumatic attacks were known. For one day before admission she was taking tincture of digitalis, ♏ xv three times daily, and for four days before that she was taking some brownish bitter medicine, the character of which we were unable to determine, in teaspoonful doses three times daily. The patient stated that this was given for her heart.

Examination showed an emaciated woman of about forty-five years who was very dyspneic and was coughing. Temperature 100° F., pulse 96 and regular, respirations 24, and blood pressure 150/115 mm. Râles were heard at both bases.

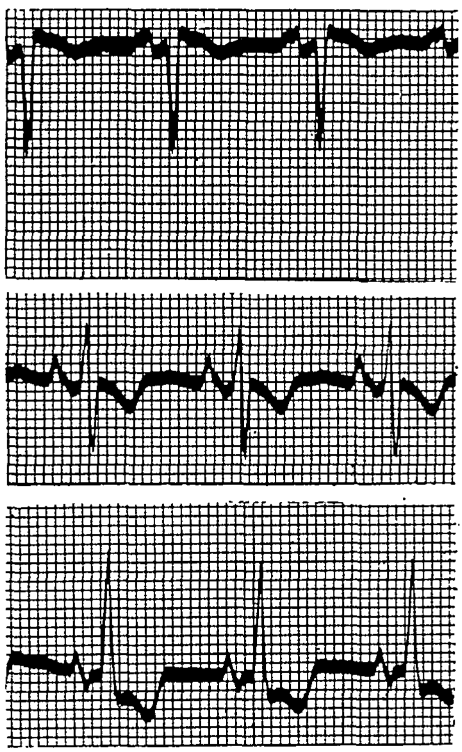

Fig. 4.—Case 2. March 26, 1929. Sinus rhythm with rate of 68. P-R interval 0.16 second. P-wave is notched in Leads I and II and diphasic in III. T-wave is inverted in all leads and is typical of digitalis intoxication. Right axis deviation.

Heart was enlarged, and there was a rough presystolic murmur and a soft systolic murmur at the apex with reduplication of the second tone throughout. There were no irregularities. The liver was down 8 cm., and there was edema of the legs. The diagnosis made was rheumatic heart disease with a double mitral lesion and heart failure, and possible recurrent endocarditis to account for the slight fever. The next day she began to have pain in the left knee, and a diagnosis of arthritis was made. The fever continued for several days. The white blood count on admission was 16,200. Urine showed ++ albumin.

Blood chemistry was normal. The Wassermann test was negative.

The patient was given tincture of digitalis, ♏ xx three times daily. On March 17 the patient showed frequent extrasystoles, but the pulse rate was 100. Digitalis was continued. On March 19, four days after admission, an electrocardiogram showed complete A-V dissociation with regular ventricular rate of 96 and an

auricular rate of 94-100 (Fig. 3). Digitalis was stopped March 23, 1929. The rate then was 84 and regular. The heart findings were the same, and the general condition was improving. On March 26, three days after stopping digitalis, the electrocardiogram showed sinus rhythm with a rate of 88 and a P-R interval of 0.16 second (Fig. 4).

DISCUSSION

It is well known that in cases of auricular fibrillation when complete heart-block supervenes (as, for example, in digitalization) bradycardia usually is present, but not infrequently relatively rapid ventricular rates may occur. The possibility that similar ventricular tachycardia may occur in cases where auricular sinus rhythm exists seems to have received little attention. Luten believes that in his four cases digitalis was responsible for the changes in conduction, and in our first case we feel reasonably certain that the large dosage of digitalis produced the complete block with the hyperirritability of the ventricles. In our second case, like one of those reported by Carr and Reddick, it seems possible that a combination of toxins—digitalis and a toxin of the rheumatic infection—produced the changes.

It is generally recognized that digitalis can produce complete heart-block, but the mechanism of its production is not clear.[4] Luten[2] in studies on cats has pictured the sequence of events in digitalis poisoning as follows: (a) inversion of the T-wave, (b) depression of A-V conduction and slowing of the heart rate, (c) acceleration of the auricles and ventricles, (d) complete A-V dissociation with a ventricular rate higher than that of the auricles, (e) abnormal ventricular rhythms, (f) ventricular fibrillation and death. Crawford[5] says that "in the advanced stages of digitalis poisoning it is known that ventricular extrasystoles appear and that ventricular tachycardia may supervene. This is due to a direct action of digitalis on the heart muscle which may cause a focus in the ventricle to give out impulses at a greater rate than the normal pacemaker, so that the former controls the ventricular rate." In our two cases, two phenomena are evident—complete A-V dissociation resulting from depression of A-V conduction, and hyperirritability of the ventricles with the development of a single focus in or near the A-V node.

We have mentioned two factors which may be responsible for the production of the changes in the heart activity described, i.e., digitalis and the existence of an acute infection. Another possible factor in our first case was the uremia, the patient having been in partial uremia for several days, although at the time the electrocardiogram was taken the uremic manifestations had disappeared. Mohler[6] in a recent article has called attention to the interesting association of uremia and heart-block, recording a case in which the A-V dissociation appeared during

uremia, disappeared with clearing of the uremia, and returned with the recurrence of the uremic state. In this case the ventricular rate was 30.

In recording these two cases, we wish particularly to point out that the presence of complete heart-block may be completely masked clinically by the existence of a relative ventricular tachycardia. In neither case reported was bradycardia present, and the rhythm was always regular except in the second case where the development of complete heart-block was preceded by numerous extrasystoles. There was nothing beyond the electrocardiograms to suggest heart-block.

We wish to thank Drs. W. W. Hamburger, Sidney Strauss, and W. A. Brams for their kind help in the preparation of this paper.

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STANDSTILL OF THE HEART OF VAGAL ORIGIN

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INSTANCES of standstill of the heart due to vagal inhibition are rare. The case to be reported is of interest as an example of this condition. Moreover, the immediate cause of the excessive vagal tone responsible for bradycardia and standstill in this patient is believed to be primarily psychic.

CASE REPORT

History.—The patient, a young man of twenty-two years, came to this clinic on June 16, 1928. Save for the fact that his father had died of pulmonary tuberculosis, the family history was negative. The boy's mother was sure he was not a "blue baby." During early life the child was sickly, but save for a severe attack of whooping cough he had no serious illness. He had frequent attacks of tonsillitis. As a child he was difficult. He did not do well at school and could not get along with the other boys. Only during the past two years had he become more sociable. While attending a private school at sixteen years of age he had an acute attack of illness which began with vomiting and diarrhea. Prior to this, he had been suffering from constipation. He was removed to a hospital where he improved, but one week later he suddenly had a "stroke" which affected his speech and the entire right side of the body. After this accident he remained at home for two years and then returned to school for a year. When at home he did out-door work or helped in a wholesale grocery. His general physical development was quite remarkable. Before the onset of his present illness he could lift sacks of sugar weighing 140 pounds without difficulty. Last spring the boy was advised to take up woodworking, and he became a carpenter's helper. However, instead of spending his time in the shop learning cabinet making as he desired, he was obliged to work outside, and his usual task was the digging of post holes. He suffered from generalized aching as a result of this exertion, but no dyspnea or symptoms of cardiac embarrassment. He thoroughly disliked the work, and his employer complained that he did not do enough. Before taking this job he had worked irregularly and was in the habit of sleeping very late each morning. During the latter part of April he was obliged to give up work because of weakness, generalized abdominal pain and fatigue. He was kept in bed for six weeks and given only a liquid diet. Three weeks before coming here he began to have frequent slight syncopal attacks. He had one severe attack when it was said that his face became black and he could not talk. When first seen here he complained that his "head got hot at times" and "things seemed to fuse together." Short spells of dizziness were frequent and also mild syncopal attacks in which "things seemed to float away." At no time while under observation did he faint or actually become unconscious.

Examination.—The boy's general appearance was normal and his muscular development was excellent. His usual weight was 140 pounds. There was still evidence of the former right hemiplegia. The right leg was dragged slightly when walking.

The right arm was held in an awkward position and movements were clumsy as though the arm were stiff, but there was no real spasticity. The reflexes on this side were increased, and there was a positive Babinski sign on the right foot. Strength was not impaired, and the right arm showed greater power than the left. The principal abnormal findings were in the heart. This was enlarged so that the left border was almost at the anterior axillary line. The total transverse diameter was 17.2 cm. There was a systolic murmur at the apex, and a short early diastolic murmur was heard in the fourth left interspace near the sternum. The first sound was of booming quality, and the pulmonic second sound was accentuated. There was no thrill. The fluoroscopic examination showed considerable enlargement of the left auricle in both the anterior and right oblique positions. The physical and roentgenographic examinations were indicative of advanced mitral stenosis, although the possibility of congenital heart disease must be considered. The blood pressure was usually low. The systolic varied from 90 to 128 mm. and the diastolic from 45 to 70 mm. The veins of the neck, head, and extremities were usually distended. Cyanosis was usually slight, appearing only in the finger nails. The lungs were normal and the vital capacity was 4150 c.c. At no time have signs of myocardial insufficiency been observed.

All of the many laboratory examinations made gave entirely normal findings. The blood calcium was 11.1 mg. per 100 c.c.

The mental status of this patient was decidedly abnormal, but difficult to classify. According to the Binet scale his mental age was fifteen years, a figure which seemed rather flattering. He was unstable, lacked power of concentration and was highly emotional. His lack of general knowledge could be accounted for in part by his limited schooling. A few examples of behavior will perhaps afford better insight into his character. When he first came to us, he exhibited a childlike interest in electric locomotives and made himself a nuisance to two corporations by his demands for photographs and drawings. Another interest was his trumpet, and almost daily he went to a near-by woods where he struggled with simple tunes. He again took up woodworking and spent hours in the carpenter shop gluing pieces of wood together. On his return home a shop was fitted for him, and this proved of definite therapeutic value, as he displayed some aptitude for woodworking on a small scale and has applied himself to it for months. These instances will suffice to indicate conduct that is certainly abnormal for a man of twenty-three years.

THE CARDIAC MECHANISM

The dominant cardiac rhythm was a pure nodal rhythm with a short R-P interval. Cases of permanent nodal rhythm are very rare and are of interest from the standpoint of that mechanism. Many examinations were made during the course of a year and a true nodal rhythm was the only one recorded. No explanation for a permanent nodal rhythm can be offered in this case, but it is reasonably certain that the vagus nerve was not responsible for it. When sitting quietly in the laboratory, the rate varied from 32 to 86 beats per minute. In a few records deflections were seen suggesting isolated auricular waves (Fig. 1, Lead III), but at no time was a ventricular response to an auricular impulse observed. The first electrocardiogram was taken on June 21. It showed a regular nodal rhythm, rate 69. To confirm the nodal rhythm, a record was taken the following day which is reproduced in Fig. 1. On June 29 many records were taken; periods of standstill varying from three to seven seconds occurred at frequent

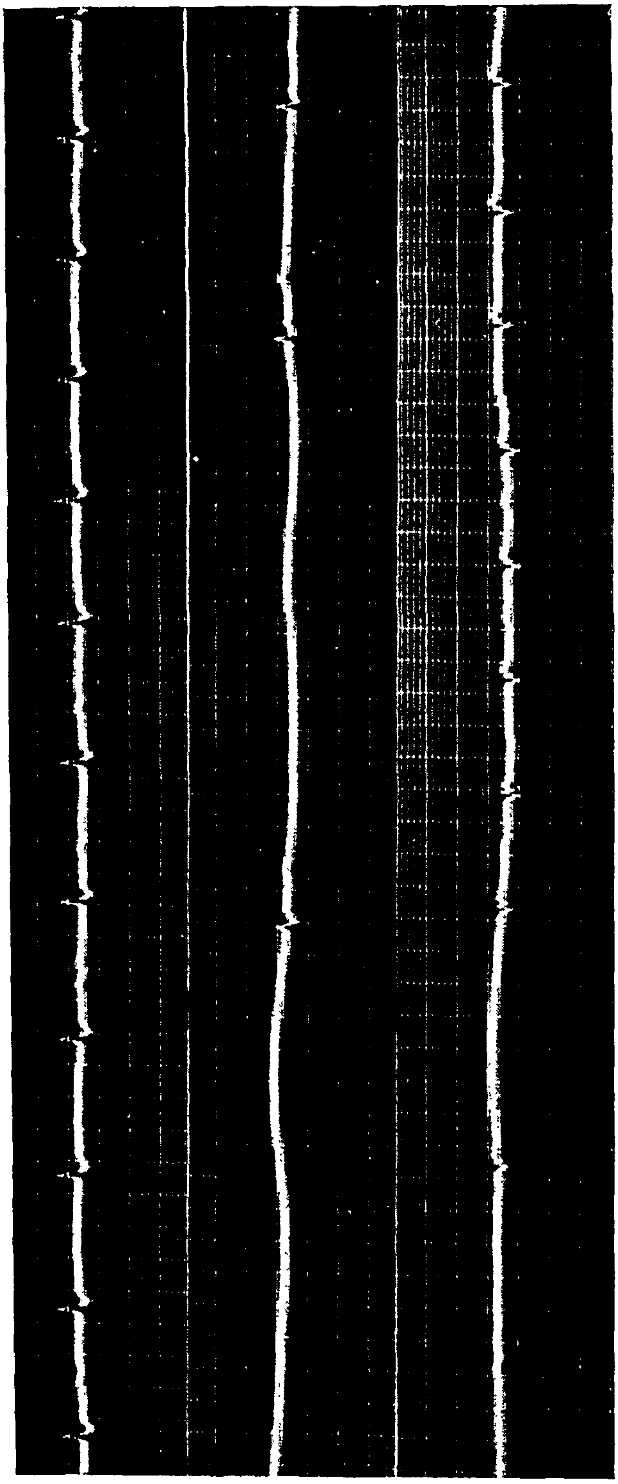

Fig. 1.—Electrocardiogram of June 22, 1928. Lead I, rate 74. Lead III, rate after pause, 83 per minute.

but irregular intervals. At several examinations made during July such pauses of the heart were always present. Then they disappeared, and the electrocardiograms made from July 18 to September 28 showed only nodal bradycardia with a rate varying from 32 to 54 beats per minute. During September the boy went home for one week. He said that after boarding the train the pauses in his pulse recurred and were frequent during his stay at home. After he returned to the clinic they disappeared promptly. On September 18 and on November 5, periods of standstill were again present. On the latter date their appearance followed an impulsive decision to return home immediately.

On days that these pauses were present the boy usually complained of slight dizziness and blurring of vision which occurred at irregular intervals. The only objective sign of the pauses was alternate paling and flushing of the skin, especially that of the face. Certainly one must conclude that cerebral anemia in this patient was very well tolerated. He was not always conscious of periods of standstill of the heart; on July 12, he said he felt very well and was not having pauses, but when electrocardiograms were taken, there were frequent periods of standstill of which he was not aware. Definite precipitating factors could be observed for some of these periods of standstill; at the first examinations they were apt to be preceded by a contortive bending backward of the trunk, and at the same time swallowing movements and deep irregular breathing were observed. On September 28, when electrocardiograms were being taken, if (from the galvanometer room) the boy were sharply commanded to sit still at a time when he was perfectly quiet and the heart was beating regularly, standstill of the heart invariably occurred. It had also been noticed that a scolding was apt to precipitate a series of pauses in the pulse. On those days when such pauses were present, they were by no means constant. They have been observed when the boy was applying to a nurse for some medicine for relief, and when he was seen a short time later on the street or in the carpenter shop, his pulse was regular, at a rate of 70 to 76 beats per minute. Even when standstill did not occur, on the taking of the pulse there was a marked fall of rate after the first ten seconds. On April 16, 1929, when the boy was becoming restless under the institutional regimen and was about to return home, the three variations of mechanism which he exhibited were recorded within less than ten minutes. It was as though constantly increasing vagal stimulation were being applied. The first record showed the usual nodal rhythm, rate 59 per minute; then periods of standstill were present for a few minutes, and these in turn were replaced by regular bradycardia, rate 36 per minute (Fig. 2).

The rates of beating at which standstill occurred varied from 63 to 86 per minute. In general the periods of standstill were longer with the slower rates of beating (58 to 70 per minute), indicating a rela-

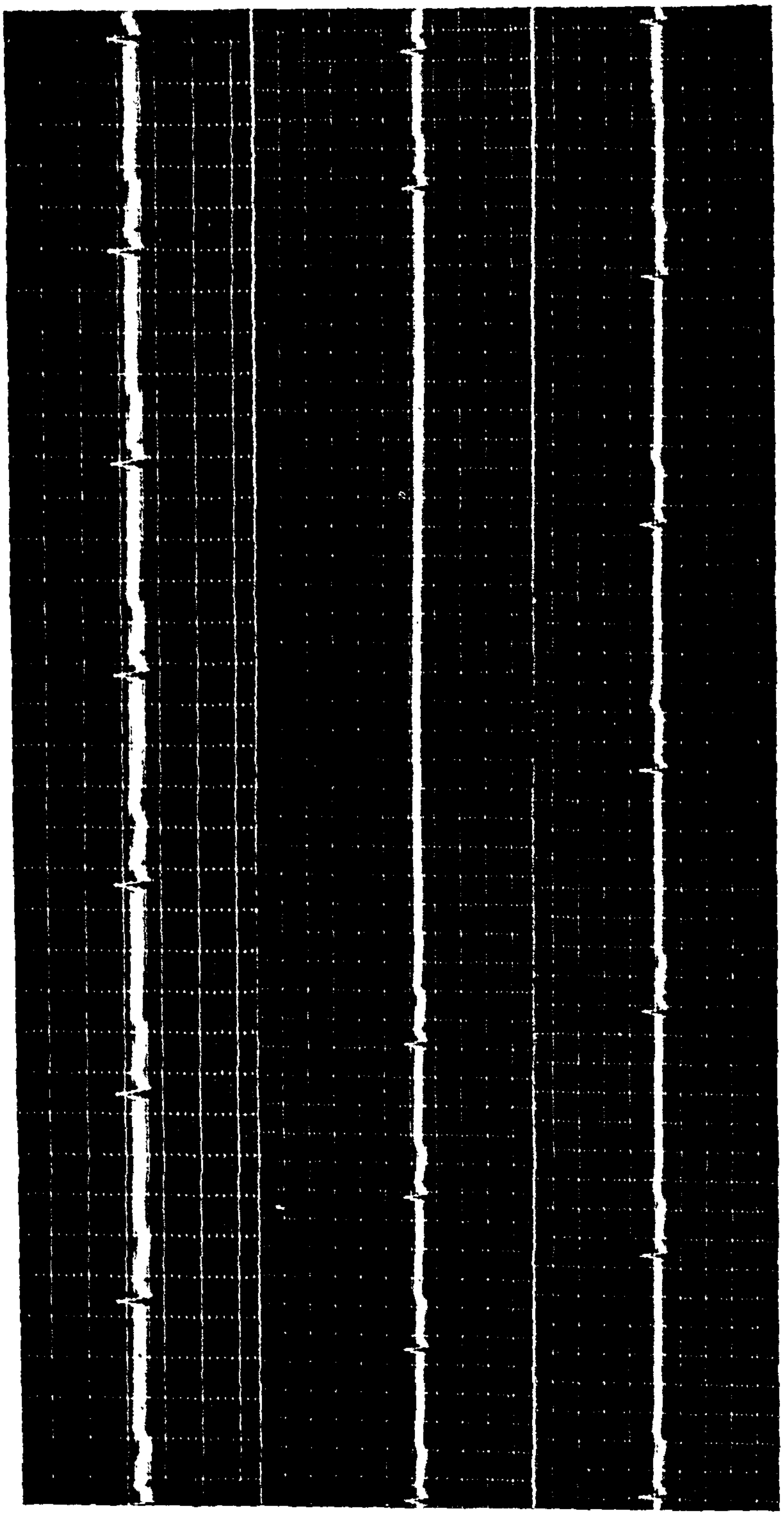

Fig. 2.—Records, (Lead II) of April 16, 1929, taken within ten minutes. Upper: rate 59 per minute. Middle: long R-R interval, 5.9 seconds. Lower: rate 36 per minute.

tively greater sustained increase in vagal tonus. They were never seen when the rate was under 45 beats per minute. Sometimes the period of standstill was preceded by slight slowing; more often it occurred abruptly. Likewise, the "pick-up" after the pause was prompt, and often the rate immediately following was slightly faster than that preceding the standstill. Occasionally after a pause of from three to four seconds a single beat was followed by a second pause, so that there was but one beat in a period of from seven to ten seconds. Only once in the many electrocardiograms taken was an altered ventricular complex seen which suggested ventricular escape.

Respiration.—On several occasions when periods of standstill were occurring, electrocardiograms and respiratory tracings were recorded simultaneously. No definite relation between respiratory movements and standstill could be ascertained. Standstill often occurred during quiet breathing, as well as after deep inspiration. At a time when periods of standstill occurred spontaneously they could be precipitated by having the patient hold his breath. But when there was present a regular bradycardia with a rate approximately 40 per minute, suspension of respiration did not cause either the appearance of periods of standstill or further slowing of the rate.

Exercise.—The response to mild exercise was always normal. Periods of standstill disappeared for a short time at least. The electrocardiograms taken on September 28 before and after exercise, which consisted of running up and down the corridor, are reproduced in Fig. 3. The rate before exercise was approximately 70 per minute with periods of standstill varying from five to six and five-tenths seconds. The rate of the first beats that could be recorded after exercise was 96 per minute; within ten seconds the rate of beating had fallen to 72 per minute. A few minutes later when the blood pressure was being taken, the pauses again appeared. On September 18, the rhythm was a nodal bradycardia, rate 41 per minute. After running down and up two flights of stairs the rate of the first recorded beats was 73 per minute; this declined rapidly to 60 per minute. The only change in the electric complexes was a decrease in the height of the R-waves at the rapid rate of beating.

Vagal Pressure.—Neither pressure in the neck over the carotid sheaths or pressure on the eyeballs produced any effect. The very attempt at such procedures resulted in a prompt fall in rate before actual pressure was applied.

Atropine.—On June 29, 1/50 grain of atropine sulphate was given subcutaneously. The maximum rise in rate occurred after twenty minutes (Fig. 4). The periods of standstill disappeared ten minutes after the injection and did not reappear that afternoon. After the full atropine effect was obtained, neither deep breathing, holding a full inspiration nor any of the contortions which before always resulted in

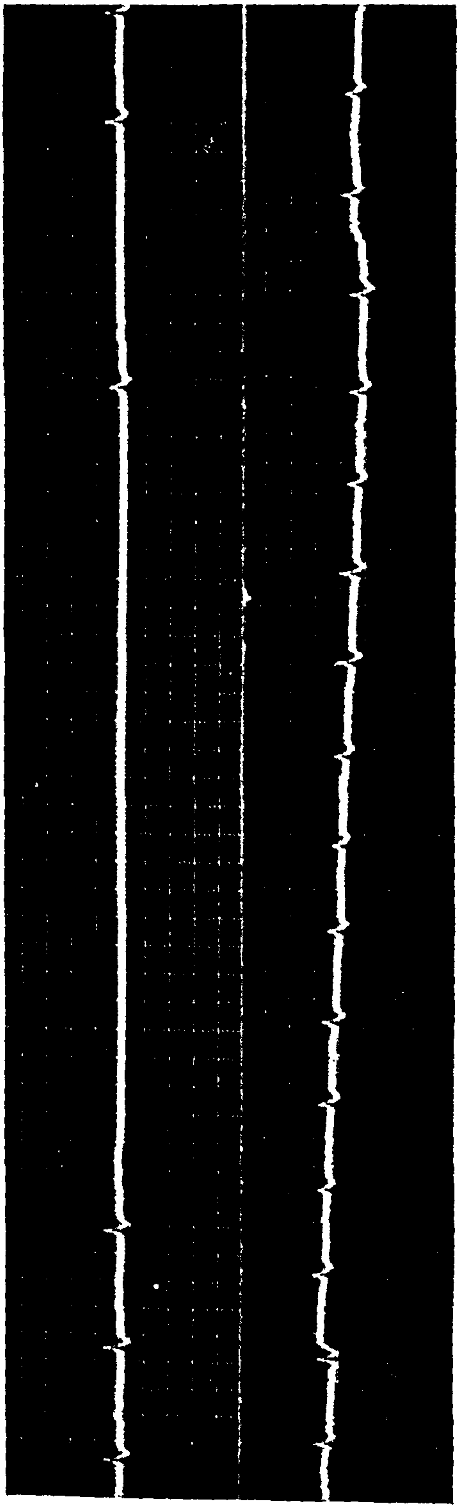

Fig. 3.—Records taken September 28, 1928, before and after exercise.

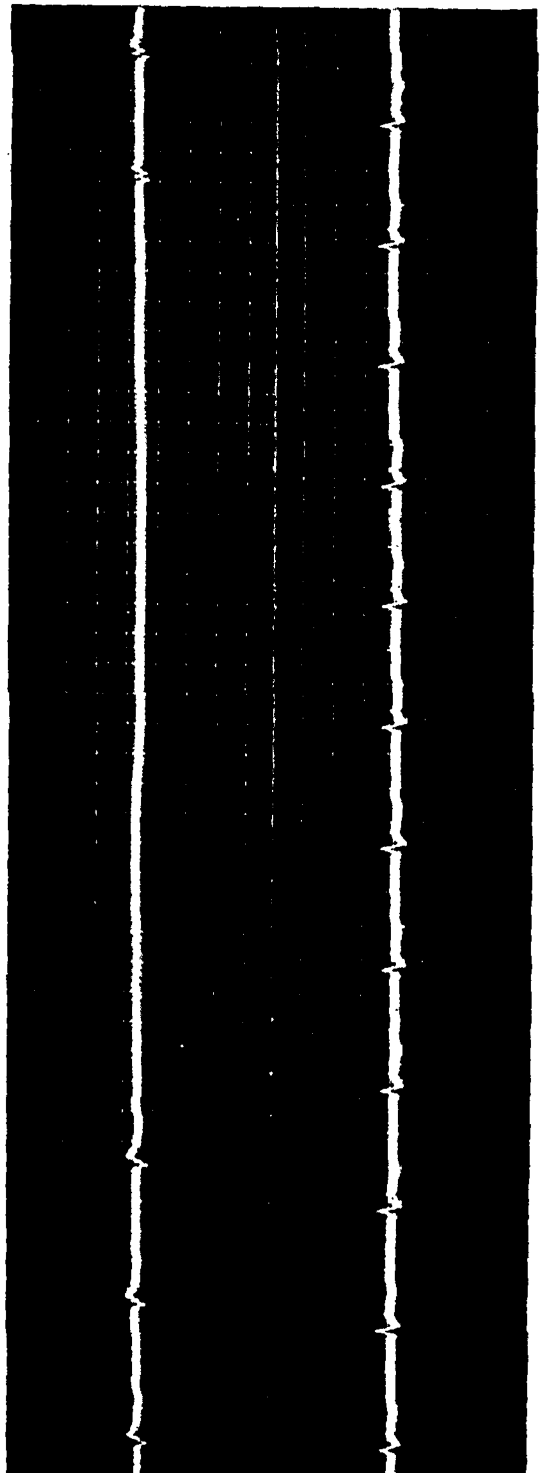

Fig. 4.—Records of June 29, 1928, before and after atropine. Long R-R interval, 6.6 seconds. Rate twenty minutes after 1/50 grain atropine sulphate, 83 per minute.

a period of standstill, caused a change in the mechanism. On August 4, $\frac{1}{50}$ grain of atropine sulphate dissolved under the tongue produced no effect whatsoever. The reaction to $\frac{1}{33}$ grain of atropine sulphate given on August 22 when nodal bradycardia was present is given in Table I. Of special interest is the definite rise in blood pressure.

TABLE I

REACTION TO ATROPINE

TIME	RADIAL RATE	BLOOD PRESSURE	E. K. G. RATE	REMARKS
2:15			39	Nodal rhythm. Slight irregularity.
2:20	42	100–48		Pulse irregular.
2:25			40	More regular.
2:30	40	95–48		
2:33	Atropine sulphate 0.03 grain (subcutaneous)			
2:48			85	No change in R-P interval.
2:53	86	120–70		
3:03			87	Face flushed.
3:08	84	128–80		
3:18			86	
3:20	82	116-76		
3:33			83	
3:37	80	110-75		Dryness of throat. Pupils widely dilated.

Epinephrin.—On August 10, nine minims of a 1-1000 epinephrin solution were given subcutaneously. This was without any definite effect; a rise in rate of six beats per minute occurred after one-half hour, but this may not have been due to the drug. On August 15, 1 c.c. of 1-1000 epinephrin solution was given, also subcutaneously. The initial rate of beating was 38 per minute. Eight minutes later the rate was 44 per minute and one extrasystole was recorded. Forty minutes after epinephrin the rate was 52 per minute; there was definite arrhythmia; the R-R intervals varied from 0.9 to 1.3 seconds; both P- and T-waves were larger. The blood pressure did not change during this observation. However, each time it was taken the boy leaned back and took a deep breath. It seemed that vagal tone was so great that it could readily offset any increase in sympathetic tone that might have been supplied by the epinephrin. Later, 1 c.c. of 1-100,000 solution was injected intravenously without any definite effect on either blood pressure or pulse rate.

COMMENT

The response of the cardiac mechanism to exercise and to atropine is conclusive evidence that both the high grade bradycardia and the standstill of the heart were of vagal origin. There remains to be considered only the question of the nature of the unusual inhibitory action. The boy had had a cerebral accident resulting in an hemiplegia. It seemed certain that this was due to a lesion in the internal

capsule and that there was no involvement of bulbar nuclei. That there could be any relation between this old injury and the present vagal disturbance seems very doubtful. There was no evidence of any lesion along the peripheral path of the vagus, as in one of Gerhardt's[1] cases, in which the left vagus nerve was imbedded in a tumor mass. Mackenzie[2] has reported standstill of the heart by vagal inhibition which resulted from digitalis medication. It is reasonably certain that drug was not a factor in the first periods of standstill that were observed. No digitalis was given during the following ten months, but periods of standstill were frequently recorded. In 1921, Wedd[3] reported a series of cases showing abnormal vagal tone which he thought had its origin in the diseased myocardium or aorta. Such a conjecture might be made in this case; organic disease was present, but in contrast to those earlier cases, the functional capacity of the heart was excellent at the time of the disturbance.

The question of an augmented vagal tone acting on a damaged conduction system may be considered. Structural changes or impaired nutrition in the A-V node or conducting system as a factor in the production of standstill of the heart seems, however, unlikely. The highest rates of beating, indicating increased rate of impulse formation in the A-V node, were seen after exercise, and at this time periods of standstill disappeared. If functional impairment in the structures concerned were a factor, some form of block should have appeared when the rate increased. The period of increased rate of beating which occasionally followed standstill was probably due solely to a decrease of vagal tone and not primarily to an improved nutritional state following the period of rest.

Perhaps the explanation of the disturbed mechanism is actually much simpler than has been implied in the foregoing paragraphs, and greater emphasis should be placed on the receptor than the stimulus. The fact that the dominant rhythm is nodal may be of prime importance. Lewis[4] states that "the influence of both vagi over rhythms emanating from the A-V node is powerful". But it can hardly be doubted that the patient had markedly enhanced vagal tone, and although considerable variation in the rate of impulse formation may occur, cessation of activity for periods of several seconds is not one of the attributes of nodal rhythm.

A search of literature has revealed very few case histories similar to the one reported here. Trocmé[5] has reported a patient with organic heart disease and periods of standstill of vagal origin, but no evidence was offered that the standstill was due to psychic factors. Laslett[6] described one instance without definite heart disease. As to the ultimate origin of the increased vagal tone he said one could express no decided opinion. Dejerine[7] states that emotions may produce syncopal crises. Gerhardt cited the case of a woman with a large heart and

disease of the conducting system in which he believed that syncopal attacks resulted from vagal stimulation and that psychic influence was the cause.

The case here reported was under almost continuous observation for ten months. Abnormal behavior of the cardiac mechanism has been so definitely related to emotional states that we feel that the only explanation for the disturbances, either the periods of standstill of the heart or the high grade bradycardia, that is consistent with all the known facts makes their origin a psychogenetic one. Because there was apparently a profound disturbance associated with organic disease, this explanation at first seems difficult to accept, but perhaps it will be less so if one bears in mind that it is not the character of the reaction but the degree that is unusual.

SUMMARY

A case is described which exhibited permanent nodal rhythm, with periods of standstill of the whole heart and of high grade bradycardia. The disappearance of these unusual disturbances of rhythm following exercise and atropine is proof of vagal origin. From a consideration of the mental and emotional make-up of the patient and of the circumstances associated with increased vagal tone it seems certain that the primary factor was a psychic one.

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ELECTROCARDIOGRAPHIC CHANGES IN QUIESCENT RHEUMATIC DISEASE IN CHILDREN AND YOUNG ADULTS*

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IN RECENT years there has been a lively interest in the electrocardiographic changes noted during acute rheumatic fever.[1-6] Several investigators have reported their work on this subject, and the conclusions drawn are quite similar. Pathologically, it is well known that in a number of instances the myocardium as well as the endocardium is involved in the acute process during rheumatic fever, but persistent evidence of these changes is often missing in post-mortem studies of chronic rheumatic heart disease. With the aid of the electrocardiogram, however, some evidence of change in the myocardium was found in almost every case of acute rheumatic fever during the acute stage. The electrocardiographic changes observed were of three main types:

1. Prolonged duration of the P-R interval, usually not to the degree of causing actual heart-block.

2. Alteration in the ventricular complex affecting either the QRS, the R-T, or S-T interval or the T-wave itself.

3. Numerous irregularities in cardiac rhythm.

Probably the most characteristic changes noted occurred in the R-T or S-T interval, these being of several different types. In some instances, the normal iso-electric period between the R-T or S-T wave was found shortened or entirely absent. Other tracings showed the R-T period coming off higher or lower than the base line. Occasional tracings showed what appeared to be an interruption of the R-wave so that the R-wave did not reach the base line but was apparently merged over with the T-wave, this change suggesting the wave described by Pardee[7] as a sign of blocking of the coronary artery. All these changes varied from time to time, and most of them disappeared, as the patients recovered from the acute stage of the disease. There was no correlation found between the electrocardiographic changes and the clinical findings. The average percentage of changes noted in the tracings by the several investigators was as follows:[5]

P-R in excess of 0.21 sec.	21.15 per cent
P-R in excess of 0.20 sec.	87.6 per cent
Changes in ventricular complex	63.5 per cent

*From the Lymanhurst School Heart Clinic, Department of Public Welfare, Minneapolis, Minn. Preparation of the illustrative material through the courtesy of the Department of Medicine, University of Minnesota.

Changes in S-T	Many to 42.4 per cent
Some change in the tracing	70.66 per cent
Extrasystoles	25.28 per cent
Dropped beats	7.7 per cent

The variations were found to be transient by most of the authors. Reid and Kenway found the changes transient in 15, or 57 per cent, of their cases. The conclusions drawn from these reports are that the changes found are characteristic of cardiac involvement but are not specific for rheumatic fever and that it will be necessary to study the cases over a longer period of time before these observations can be used clinically for diagnosis and prognosis.

Thus it seemed worth while to study the electrocardiographic changes during quiescent rheumatic disease in children and young adults who had apparently recovered from the acute rheumatic process. In following over a period of six years more than 300 children and young adults who gave a previous history of rheumatic fever or chorea or both, it was noted that the infectious process does not always cease when the patient is permitted out of bed but that definite signs of a low grade continuous infection are present. A large number of these children have almost a continuous rise of temperature to 100° F. or above; they have frequent attacks of "growing pains"; they have occasional attacks of a single swollen joint; leucocytosis of a low grade appears from time to time; the pulse is rapid at rest, and the children are often anemic. Electrocardiographic tracings were taken on 119 children who were attending the Lymanhurst School Heart Clinic. The tracings were repeated from time to time, but because of the character of the material it was not possible to obtain repeated tracings on all of the children. Twenty per cent of these children gave a history of rheumatic infection during the two previous years. Sixty-five per cent had their acute rheumatic disease within three years from the date of the first tracing. Eighty-seven, or 73 per cent, of these children had definite rheumatic heart disease, while thirty-two, or 27 per cent, showed no involvement of the heart as far as could be determined by clinical examination or x-ray. The majority had been confined to bed for varying periods of time, and in practically every case the diagnosis of rheumatic disease had been made by the attending physician. The tracings were all made at the Minneapolis General Hospital and for the most part were read by Dr. M. H. Nathanson of the staff of that hospital.

These tracings revealed the following findings:

1. *Changes in P-Wave.*—In five cases, or 4 per cent, a distinct notching in the P-wave was found in the first or second lead or both and also in five tracings, or 4 per cent, the P-wave was unusually high or peaked.

2. *Changes in P-R Interval.*—In ten patients, or 8 per cent, the P-R interval was prolonged to 0.2 sec. or more, but in no instance was this sufficient to produce an actual heart-block.

3. *Changes in QRS Complex.*—In four cases, or 3 per cent, the QRS period was notched at the peak in the first or second lead or both, and in four instances, or 3 per cent, the QRS was widened to 0.12 sec.

4. *Changes in R-T or S-T Interval.*—(Figs. 1 and 2.) In fifty-three cases, or 45.5 per cent, the isoelectric period was entirely absent, and the T-wave actually came off directly from the descending limb of the R-wave or the S-wave. In twenty-one, or 17.5 per cent, of the cases the R-T or S-T interval was definitely shortened; the rise was distinctly abrupt; there was practically no iso-electric period. The iso-electric period was either entirely absent or markedly changed from normal in

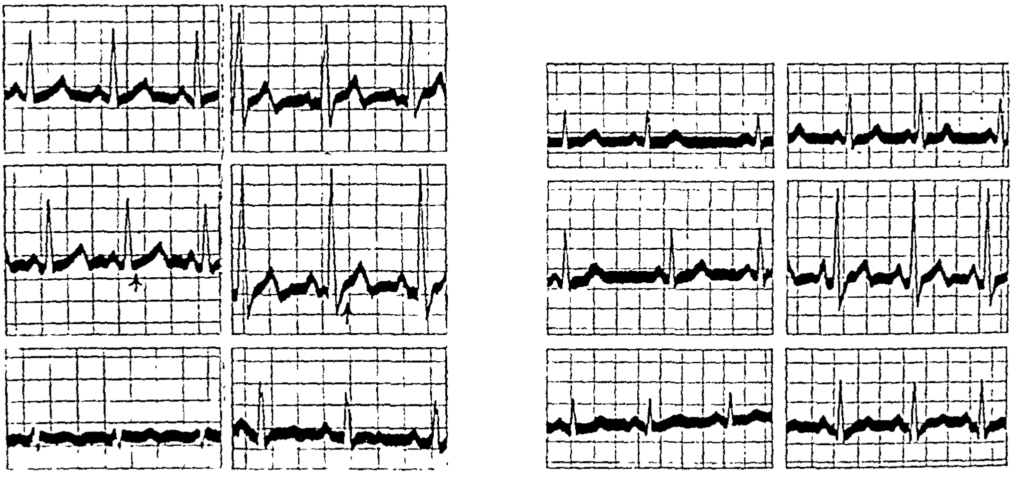

Fig. 1-*B*. Fig. 1-*A*. Fig. 2-*A*. Fig. 2-*B*.

Fig. 1.—Absence of normal isoelectric period between the R-T or S-T interval.

Fig. 2.—Tracings on one patient on different dates, showing variations in R-T or S-T interval.

63 per cent of the cases studied. In eighteen cases, or 15 per cent, the T-wave came off higher than the foot points of the R-wave, while in twenty-three, or 19 per cent, the T-wave had its inception lower than the base line. In ten tracings, or 8 per cent, the R-wave was interrupted in its progress toward the base line, the T-wave starting as a direct continuation of the interrupted R-wave, suggesting the change which frequently has been described as indicative of coronary occlusion (Fig. 3).

5. *Changes in the T-wave.*—In three instances the T-wave was negative in Leads I or II or both.

6. *Arrhythmia.*—Two instances of auricular extrasystoles and one of ventricular extrasystoles were noted as well as eight instances of sinus arrhythmia.

In order to determine whether or not these same changes might be present in tracings taken from children with normal hearts who gave no history of rheumatic infection a single tracing was taken on each of 50 children, who were examined in the Minneapolis Public Schools and found to have normal hearts and who gave no history of rheumatic disease. In none of the electrocardiographic tracings taken in this control group was the P-R interval prolonged to 0.2 sec., and there were no significant notchings or widening of the QRS complex.

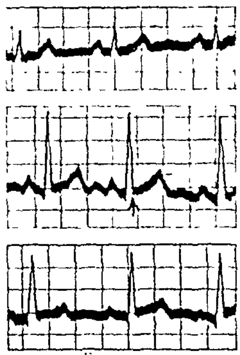

Fig. 3.—The descending limb of the R-wave does not reach the base line suggesting the change described as typical of coronary occlusion.

Fig. 4.—Tracings on one patient taken on different dates, showing changes in R-T or S-T interval as well as decided variations in the T-waves and some change in the QRS complexes.

In three instances the S-T interval was shortened more than is usually considered normal, but in none of this control group was there an entire absence of the iso-electric period between the R or S and the beginning of the T-wave. There were no inversions of the T-wave in Leads I or II, nor were there any irregularities in cardiac rhythm other than eight instances of sinus arrhythmia.

In order to determine whether or not the variations in the tracings found in acute rheumatic fever might also exist in tracings taken on children with quiescent rheumatic disease, twenty of these children, who gave a definite history of rheumatic infection, had repeated trac-

ings taken over a period of a year. A control group of ten of the normal children also had repeated tracings. This group is too small for statistical treatment; however, the differences between these two sets of tracings were striking. In the normal group the tracings remained practically unchanged, while those taken on the rheumatic group varied considerably from time to time. The P-wave became notched where before it was not notched; the S-wave became deeper in one or more leads; notching appeared in the QRS complex; the T-wave became diphasic, flattened or inverted where before it had been positive; the T-wave also in many instances came off higher or lower than previously, and there were also other minor variations in the S-T or R-T interval (Fig. 4).

It is, therefore, apparent that the variations in this quiescent rheumatic group are similar to the changes found by other investigators studying electrocardiographic changes during acute rheumatic fever.

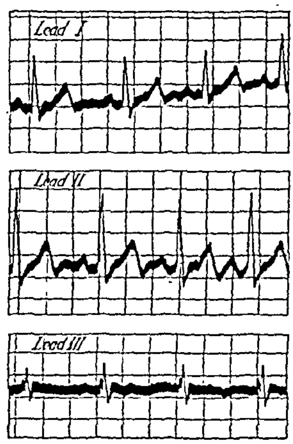

Fig. 5.—Tracing taken on March 12, 1928, when diagnosis was functional heart disease. This child subsequently developed a characteristic mitral stenosis. Shows absence of iso-electric interval between S- and T-waves especially well in Lead II.

DISCUSSION

The diagnosis of rheumatic carditis in the early stage is often solely dependent on the history of previous rheumatic infection, this being especially true when there is no cardiac enlargement. However, rheumatic disease is of such a variable nature that it is often difficult to evaluate symptoms presented as indicative of rheumatic disease. It is frequently difficult to decide whether or not a systolic murmur heard at the apex of a child's heart has any significance. The apical systolic murmur means more in a child than in an adult. It is not uncommon to follow children with such indefinite findings over a period of years and watch them develop into typical mitral stenosis with characteristic cardiac enlargement when in the beginning the murmur was considered as nonpathological and of no importance. As an example of such a case, the following might be cited:

A mother brought her child to the clinic, complaining that the child was not well, was pale, and had been sent home from school repeatedly because of fever, this rise of temperature having been more or less persistent over a period of weeks. Examination revealed a localized systolic murmur over the apex. The x-ray showed no enlargement of the heart, and we obtained no history of rheumatic disease nor even a history of "growing pains" or frequent tonsillitis. At that time we considered this case as functional heart disease and had the child examined carefully for a possible pyelocystitis. On re-examination a year and a half later we found a definite double mitral lesion with characteristic cardiac enlargement verified by x-ray. In this type of case the electrocardiogram would prove of more than theoretical value. In this particular instance, tracings taken when the child was first examined did show changes which were probably characteristic of rheumatic infection but were not recognized at that time (Fig. 5).

The study of tracings taken from children with quiescent rheumatic disease shows changes similar to those found during acute rheumatic fever, but the frequency of changes in the quiescent group was smaller. As in the active group, the changes varied from time to time. The most prevalent and most characteristic change noted was the absence of the isoelectric period between the S-T or R-T interval and the variability of this portion of the tracing. It is desirable to correlate the electrocardiographic changes with clinical evidence of continued rheumatic activity and to study these changes over a longer period of time.

SUMMARY

Electrocardiographic tracings were taken on 119 children giving a history of rheumatic disease who were able to attend school regularly; tracings were also taken on 50 normal children who were used as controls. Many of the tracings taken from the children in the so-called quiescent group showed changes similar to those found in acute rheumatic fever, but the changes were found less frequently. Repeated tracings taken from children in the quiescent group showed variations similar to those found in the acute group. In the control group the tracings did not vary. The most common and most persistent finding in this quiescent group was the lack of iso-electric period between the R- or S-wave and the T-wave and the marked variability of the R-T or S-T interval from time to time.

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THE DENSITY OF THE SURFACE CAPILLARY BED OF THE FOREARM IN HEALTH, IN ARTERIAL HYPERTENSION, AND IN ARTERIOSCLEROSIS*

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THE permeability and extent of the capillary bed has a fundamental bearing on tissue nutrition. While the permeability of the capillaries has been studied extensively, little is known concerning the density of the capillary bed of different organs in normal persons, and practically no information is available on the possible variation in the number of capillaries in disease. Coincident with involutionary changes of the body, a reduction in the reserve functional capacity of all organs occurs. There is also shrinkage in the volume of the tissues. The following factors referable to the capillary system may be responsible for the involutionary changes in the body: *A*, insufficient blood supply to the normal capillary bed; *B*, progressive disappearance of the capillaries with the result that cell areas of increasing radius are supplied by a single capillary; *C*, a disturbance of normal tissue nutrition as a result of impaired capillary permeability rather than a decrease in the number of capillaries; *D*, inability of the nutritive substances to reach the cells in normal proportion as a result of increase in the intercellular (cement) substances between capillaries and specific tissue cells. It is possible that various combinations of the enumerated factors may be active.

The difficulty of estimating the density of the capillary bed of human post-mortem tissues is well recognized. This difficulty is considerable even in experimental animals in which the injection of dyes may be started during life.[1, 2] Quantitative studies on the capillary content of tissues at different ages and under various conditions have not been recorded.

PURPOSE AND PLAN OF INVESTIGATION

The aim of the study presented here was to compare the surface capillary bed of an arbitrarily chosen skin area of the body of subjects without vascular disease with that of a group of patients with arterial hypertension and a group of patients with advanced arteriosclerosis. Theoretically, progressive decrease in the number of capillaries may be responsible for elevation of blood pressure and for involutionary changes in the body. The skin was chosen for study because it shows

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involutionary changes with advancing age, as judged from the change in consistency and elasticity. Skin tissue also permits observations on its capillaries in man under natural conditions. Wetzel and Zotterman[3] counted the visualized skin capillaries of various skin areas of normal subjects.

All the individuals studied were fair-skinned. Three skin areas over the antecubital surface of the forearm were selected arbitrarily for observation. The forearm was chosen because it has a delicate skin area which is only slightly exposed to changes in temperature, light and trauma, and because it is possible to immobilize it in a position convenient for microscopic observations. The arm was prepared by washing with soap and water and applying microscope immersion oil to the area to be studied. With the patient in a horizontal position, the arm was extended between two sand bags and attached to the long supporting arm of a heavily built iron stand under a capillary microscope. In order to visualize all the capillaries, the skin was congested by applying above the elbow a maintained pressure of approximately 100 mm. of mercury, a pressure just above the patient's diastolic arterial pressure. The capillary counts were started when a red flush appeared on the arm, indicating that the minute vessels were dilated. Absence of flush indicated that the congestive pressure was above the level of the systolic pressure. Because the blood volume of the arm is above normal under this experimental condition, it may be assumed that all the surface capillaries became filled with blood. This arrangement permits comparison of the capillary content of corresponding skin areas of different individuals under identical experimental conditions.

The first area (Skin Area A) observed was located 7 cm. below the epicondylar line over the lower angle of the antecubital space. The second area (Skin Area B) was 12 cm. below the epicondylar line, or approximately midway between the elbow and wrist joint. The third area (Skin Area C) was 3 cm. proximal to the lower border of the radius.

The capillaries were counted through a ruled disc inserted over the lens of the ocular of the microscope. A calibration indicated that 1 sq. mm. of the disc corresponded to 2.3 sq. mm. of skin area. After a little experience, only occasional difficulty was encountered in distinguishing the superficial capillaries from the subcapillary venous plexuses. Obviously, the microscope and forearm had to be in fixed position. Repeated counts over the same area showed a variation of less than 10 per cent as a rule. At least 5 counts were made over an area of 2.3 sq. mm. on each of the three skin areas. In addition to the capillary count, the capillaries of the nail bed were examined for their shape and for the nature of the blood flow.

To prove whether or not the presence of epidermis interferes with the visualization of the capillaries, small blisters were raised with cantharidin plasters over the upper portion of the forearm in five patients and the count over the blistered area was compared with that of the immediately adjacent area.

OBSERVATIONS

Table I indicates that the epidermis does not interfere with the counting of the capillaries.

TABLE I

COMPARATIVE COUNTS OF THE CAPILLARIES OF THE SKIN WITH AND WITHOUT THE PRESENCE OF THE EPIDERMIS

PATIENT NO.	AGE	DIAGNOSIS	NORMAL SKIN AREA CAP. PER SQ. MM.	BLISTERED SKIN AREA CAP. PER SQ. MM.
1	14	Post-rheumatic fever	30	33
2	51	Duodenal ulcer	25	27
3	59	Arteriosclerosis	25	26
4	60	Arteriosclerosis	35	33
5	60	Hypertension, arteriosclerosis	30	27
6	75	Hypertension, arteriosclerosis	28	28

Table II presents the capillary count over the three areas of the forearm of 20 control subjects with a normal cardiovascular system. Table III presents the counts of 20 patients with elevated arterial blood pressure: six of the patients suffered from essential hypertension without evidence of arteriosclerosis; the other 14 patients showed varying degrees of soft sclerosis of the peripheral arteries which probably resulted from a persistent high blood pressure. All the patients of this group had enlarged hearts. Table IV includes the capillary counts of 20 patients with senile arteriosclerosis but without hypertension or cardiac enlargement.

The capillary distribution in the patients with arteriosclerosis showed a rather marked irregularity and "moth eaten" appearance. The capillary loops of the nail bed showed irregularities, and the arterial portion of the loop was often narrow and hairlike in the patients with elevated blood pressure.

DISCUSSION

The results of these observations indicate that the capillary count was distinctly higher in the distal portion of the skin areas in both the control subjects and in the patients. The average capillary count varied between 25 and 58 per sq. mm. with an average of 35 in the normal subjects; between 22 and 49 per sq. mm. with an average of 35 in the group of patients with elevated blood pressure; and between 17 and 39 per sq. mm. with an average of 30 in the senile arteriosclerotic group.

TABLE II

THE EXTENT OF THE SURFACE CAPILLARIES OF THE SKIN IN 20 CONTROL SUBJECTS WITHOUT HYPERTENSION OR ARTERIOSCLEROSIS

SUBJECT NO.	AGE, YEARS	CONDITION	ART. BL. PR. SYST. MM. HG.	ART. BL. PR. DIAST. MM. HG.	AREA A CAP. PER SQ. MM.	AREA B CAP. PER SQ. MM.	AREA C CAP. PER SQ. MM.	AVERAGE COUNT CAP. PER SQ. MM.	VELOCITY OF CAP. BLOOD FLOW	TORTUOSITY OF CAP.
1	12	Post-rheumatic Fever	108	86	22	23	31	25		
2	14	Post-rheumatic Fever	118	84	25	30	38	31	Normal	Normal
3	15	Normal	108	70	29	31	38	33	Normal	Normal
4	16	Diabetes	116	74	27	31	32	29	Normal	Normal
5	16	Normal	112	66	31	38	43	37	Normal	Normal
6	23	Post-rheumatic Fever	136	109	23	32	45	31	Normal	Normal
7	23	G. C. Urethritis	142	88	31	33	40	35	Normal	
8	24	Post-rheumatic Fever	116	72	24	30	39	31	Normal	Normal
9	28	Post-rheumatic Fever	110	45	30	28	30	29		Normal
10	32	Aortitis	106	78	34	43	57	45		
11	35	Duodenal Ulcer	114	84	23	25	41	30	Slow	Normal
12	42	Toxic Hepatitis	120	76	28	33	46	36	Slow	Normal
13	44	Gastric Ulcer	112	78	19	33	50	34		
14	45	Psychoneurosis	116	19	25	33	41	33	Slow	Normal
15	45	Psychoneurosis	122	82	29	35	49	38	Normal	Normal
16	47	Dengue Fever (?)	92	64	31	37	55	41	Normal	Normal
17	47	Normal	114	40	34	35	50	40	Slow	Normal
18	50	Sinusitis	108	80	28	37	47	37	Normal	Normal
19	50	Pellagra	116	80	50	52	72	58		Normal
20	51	Duodenal Ulcer	98	66	20	28	32	27	Normal	Normal
Average	32.9		114.2	73.0	28.2	33.4	43.8	34.6		

TABLE III

THE EXTENT OF THE SURFACE CAPILLARIES OF THE SKIN IN 20 PATIENTS WITH ARTERIAL HYPERTENSION

PATIENT NO.	AGE, YEARS	SECONDARY DIAGNOSIS	ART. BL. PR. SYST. MM. HG.	ART. BL. PR. DIAST. MM. HG.	AREA A CAP. PER SQ. MM.	AREA B CAP. PER SQ. MM.	AREA C CAP. PER SQ. MM.	AVERAGE COUNT CAP. PER SQ. MM.	VELOCITY OF CAP. BLOOD FLOW	TORTUOSITY OF CAP.
1	18	Rheumatic Heart Disease	170	100	29	32	40	34	Rapid	Normal
2	38	None	202	110	34	39	45	39	Normal	Normal
3	40	None	210	100	30	36	38	35	Rapid	Slight
4	41	Nephroscletosis	156	168	23	33	46	34	Rapid	Marked
5	42	None	220	120	33	28	50	40	Normal	Slight
6	42	None	204	112	27	32	44	35	Rapid	Normal
7	43	Arthritis	158	110	23	27	36	29	Rapid	Marked
8	48	None	228	105	30	36	39	35	Rapid	Slight
9	52	Nephrosclerosis	196	115	29	28		28	Rapid	Normal
10	59	Cirrhosis of Liver	182	114	27	35	54	39	Rapid	Normal
11	60	Arteriosclerosis	210	110	30	36	43	36	Slow	Normal
12	62	Obesity	152	88	36	43	55	45	Rapid	Normal
13	62	Emphysema	208	100	28	28	47	34	Rapid	Normal
14	62	Cardiac Asthma	174	104	30	33	50	37	Rapid	Marked
15	64	Obesity	160	84	26	27	44	34	Rapid	Marked
16	68	Myocardial Degeneration	162	74	35	37	75	49	Slow	Normal
17	75	Arteriosclerosis	162	100	26	39	42	36	Normal	Normal
18	76	Arteriosclerosis	170	100	22	21	23	22	Normal	Normal
19	84	Arteriosclerosis	170	100	20	38	50	36	Normal	Normal
20	84	Arteriosclerosis	162	94	18	18	44	27	Rapid	Normal
Average	56		182.8	102.4	27.8	32.8	45.4	35.2		

TABLE IV

THE EXTENT OF THE SURFACE CAPILLARIES OF THE SKIN IN 20 PATIENTS WITH ARTERIOSCLEROSIS AND NORMAL BLOOD PRESSURE

PATIENT NO.	AGE, YEARS	SECONDARY DIAGNOSIS	ART. BL. PR. SYST. MM. HG.	ART. BL. PR. DIAST. MM. HG.	AREA A CAP. PER SQ. MM.	AREA B CAP. PER SQ. MM.	AREA C CAP. PER SQ. MM.	AVERAGE COUNT CAP. PER SQ. MM.	VELOCITY OF CAP. BLOOD FLOW	TORTUOSITY OF CAP.
1	50	Tabes Dorsalis	104	70	29	25	28	27		Normal
2	50	Sinusitis	124	74	26	30	39	32	Normal	Normal
3	51	Auricular Fibrillation	138	84	28	33	52	38	Slow	Normal
4	52	Alcoholic Neuritis	130	80	29	35	38	34		
5	52	Cerebral Thrombosis	114	80	35	34	42	37	Normal	Normal
6	54	Obesity	110	80	27	35	48	37	Normal	Marked
7	59	Post Pneumonia	128	75	22	25	42	29		
8	60		137	77	17	17	18	17	Slow	Normal
9	60	Scurvy	146	68	21	24	38	28	Rapid	Normal
10	61	Pernicious Anemia	114	68	31	35	50	39	Normal	Normal
11	62	Cerebral Hemorrhage	112	80	24	32	49	35	Slow	Marked
12	62	Fibroid Tuberculosis	94	68	25	25	40	30	Normal	Normal
13	65	Auricular Fibrillation	120	76	26	28	37	30	Rapid	Normal
14	68		130	84	25	29	33	29	Normal	Normal
15	70	Diabetes	144	68	23	27	39	29	Normal	Marked
16	70	Alcohol Addiction	134	80	27	26	31	28	Normal	Marked
17	71		136	84	20	24	32	25	Slow	Marked
18	73		124	70	30	35	37	34	Slow	Normal
19	72		134	80	24	24	30	26	Normal	Normal
20	74	Post Pneumonia	104	74	23	27	29	26	Rapid	Normal
Average	61.8		123.8	76.0	25.6	28.5	37.6	30.5		

The variations in the counts within the groups were considerable, but no more than in certain circulatory functions. These variations are the more natural since the count of the surface capillaries is not necessarily an index of the number of capillaries per c.mm. of skin. The graphic representation of the distribution of the counts (Fig. 1) exhibits no definite difference between the three groups of individuals. The average count of the arteriosclerotic group is slightly lower than that of the control or hypertensive group. The distribution curve of the capillary contents of the arteriosclerotic group is shifted slightly to the left as shown in Fig. 1. No relationship existed, nevertheless, between the capillary counts and the clinical evidence of arteriosclerosis. Similarly, no relationship existed between the counts and the age of the patients. The average capillary count for subjects between ten and twenty-nine years of age (shown in Tables II, III, and IV) was 33 per sq. mm.; for subjects between thirty and forty-nine years

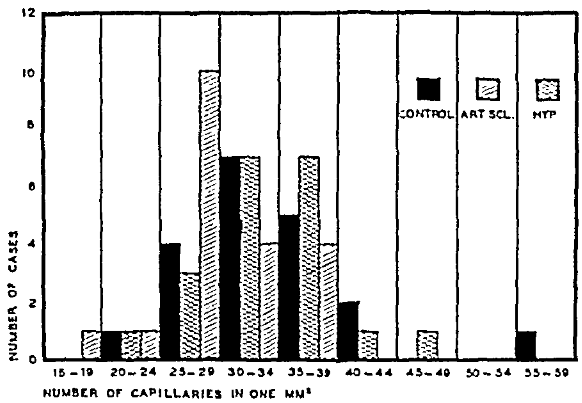

Fig. 1.—Graphic representation of the distribution of the extent of the surface capillary bed of the forearm in control subjects with a normal vascular system and in patients with arterial hypertension or with arteriosclerosis.

of age, 36 per sq. mm.; and for subjects between fifty and eighty-two years of age, 33 per sq. mm. The average count found in normal subjects was 33. The value found by Wetzel and Zotterman for the forearm was 43 per sq. mm. Their counts apparently were performed over the lower portion of the forearm.

The results of the study presented here indicate that reduction in the number of visible surface capillaries per square unit cannot be held responsible for the changes observed in the skin with advancing age and in arteriosclerosis. The radius of the cell area supplied by a single surface capillary may be the same in an aged individual with sclerosed larger vessels and inelastic, shrunken, thin skin as that in a young adult with elastic, smooth, normal skin. Since change in the number of capillaries per sq. mm. must be eliminated as a factor responsible for the involution of the skin, the responsible causes are probably among the other possibilities described above. The observation that the number of capillaries per sq. mm. is essentially the same

in patients with severe arteriosclerosis as in healthy young subjects, does not rule out definitely the possibility that a progressive decrease in the capillaries occurs with advancing age or with arteriosclerosis. If such a state of affairs exists, however, it must follow, in view of our findings, that with the loss of function of the capillaries the cells supplied by these capillaries disintegrate, and hence shrinkage of tissue follows. Thus the number of capillaries per sq. mm. remains essentially unaltered. Whether a reduction of the capilary bed and an increase of tissue radius supplied by a single capillary is not occasionally responsible for morbid changes in tissues cannot be stated from the observations presented.

CONCLUSIONS

1. The extent of the surface capillary bed of the skin of the forearm was essentially the same in a group of control subjects without vascular disease and in patients with arterial hypertension or arteriosclerosis.

2. Progressive involutionary changes of the skin cannot be explained on the basis of an increase in the radius of cell areas supplied by the surface capillaries.

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Department of Clinical Reports

LOCALIZED SWEATING, A SYMPATHETIC REFLEX PHENOMENON IN ANGINA PECTORIS

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AMONG the less usual and more interesting manifestations of angina pectoris are those symptoms the underlying mechanism of which appears to be a sympathetic reflex arc connecting the heart and aorta with visceral organs or glandular tissue. The following is the report of such a case.

CASE REPORT

A robust, somewhat florid physician of sixty-one years was seen ten days after having been awakened at 3 A.M. by severe precordial pain radiating into the left arm, lasting one hour, requiring morphine for relief. The patient had suffered two similar attacks six and two years previously. After the first attack the patient remained in bed three days and returned to his practice after five days, though he experienced precordial pain or substernal gripping on hurrying, usually relieved by rest. This passed away after four months and he tolerated strenuous exercise, even playing tennis without discomfort. After the second attack two years before, the patient led a somewhat less strenuous life though continuing in active practice. With all three attacks he noted light-colored stools and uneasiness in the right upper quadrant.

Both parents of the patient were long lived, dying at seventy-nine and eighty-eight years respectively. One brother died of heart disease at sixty-two. One sister now has hypertension. The patient had rheumatic fever lasting one week at thirty years of age. He had influenza with pneumonia in 1918. Answers to routine questions as to previous symptoms were negative except for some indigestion, consisting chiefly of gas after meals. There was no history of frank gall bladder attacks, jaundice, or constipation.

The physical examination was negative aside from a few râles at the bases. The examination of the heart was as follows: Cardiac dullness to percussion in the fifth space was 11 cm. to the left, 2.5 cm. beyond the midclavicular line. The left border of the heart was 7 cm. to the left in the third space. The transverse supracardiac dullness was 6.5 cm. There was a moderate to loud systolic murmur heard over the precordium, best heard at the apex. The rate was 90 and a well-marked gallop rhythm was noted. The blood pressure was 145 mm. mercury systolic and 110 diastolic. Alternation of the pulse was observed.

During absolute rest in bed the patient suffered some precordial distress and some indigestion with gas. On one occasion he had pain and tenderness in the right upper quadrant and gaseous eructations during the night. This recurred the next morning after taking a cup of coffee and was accompanied by pain in the left upper chest radiating into the arm.

The most interesting symptom of which this patient complained occurred two weeks after the onset of the third attack. He awoke to find the precordium, left

shoulder and left arm to the elbow drenched with sweat. The body was of normal moisture elsewhere. There was no pain, pressure or heaviness. He noticed that his pulse rate was somewhat accelerated.

Mackenzie[1, 2] noted flushing or sweating of forehead or body with attacks of angina. Vomiting, salivation, gaseous eructations and increased flow of urine were also observed by him. Vaquez[3] mentions fleeting vasomotor phenomena in angina pectoris, such as diffuse redness of hands and forearms accompanying or preceding the attack, and refers to observations by others of this flushing extending to face and chest.

Misch and Lechner[4] have recently reported two cases showing a sympathetic reflex similar to that reported in the present case except that the area of hyperhidrosis was the left side of the face supplied by the upper two branches of the trigeminal nerve. One of these patients had luetic heart disease, aortitis, aortic regurgitation and angina pectoris. The second patient was diagnosed as coronary sclerosis and angina pectoris. Both patients showed dilatation of the left pupil. These same authors refer to two other cases. One of these, similar to the subject of the present report, was described separately by Conzen[5] and Bittorf.[6] A woman forty-six years of age had attacks of angina pectoris and occasionally with these attacks flushing and sweating of the left side of the face. The left pupil was twice as large as the right and was known to have been so for ten years. Gibson's[7] patient was a man forty-five years old who complained of constant pain in the left upper back and chest and in the arm with exacerbations of greater severity, relieved by amyl nitrite. This patient showed prominence of the left eye and dilatation of the left pupil, changes of which were more marked during attacks of pain. There was no sweating or skin changes except some pallor during an attack. The patient's symptoms improved under potassium iodide. X-ray examination of heart and great vessels was negative.

These cases clearly represent a reflex from the heart or aorta to the sweat glands, or ciliary muscle in those showing dilatation of the left pupil, conveyed by the sympathetic system and passing from the cord in the lower cervical and upper dorsal region,[8] which experimental and clinical research has shown is the pathway in typical anginal pain of the usual distribution. Head[9] produced a unilateral reflex hyperhidrosis in certain cases of gross cord injury, the stimulus being somatic, such as scratching or pinching the skin. The reflex in the above cases is evidently initiated by a visceral stimulus, namely anemia of the myocardium or a stimulus arising from aortic disease.

Recently the gastric and abdominal manifestations of angina pectoris and the differential diagnosis between cardiac and abdominal disease have claimed the attention of clinicians.[10, 11, 12, 13, 14] It is certainly very likely that a similar sympathetic reflex, the end organ

being in the abdominal viscera, is responsible for the disordered function giving rise to the symptoms. A very common and familiar manifestation is the indigestion characterized by gas, sour eructations and heartburn which so often accompanies attacks of angina pectoris or occurs with fatigue or slight overexertion in patients subject to anginal attacks. The mechanism is probably a sympathetic reflex from heart or aorta causing pylorospasm.

SUMMARY

One case is reported and three cases are quoted from the literature representing an unusual sympathetic reflex phenomenon in angina pectoris, which consists of localized sweating.

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LOCALIZED SWEATING REPLACING CARDIAC PAIN*

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THE following case is reported because it illustrates the occurrence of sympathetic reflex sweating in a patient with anginal pain. It is interesting to note that the sweating was strictly limited to the region where the patient had felt pain on effort for twenty-five years, but that the sweating occurred while the patient was at rest and not with the pain.

CASE REPORT

A.J.N., a retired clerk, aged 75 years, was admitted to the New York Hospital (service of Dr. L. A. Conner) on November 20 and died on December 21, 1926. He had rheumatic fever at 25 and at 27 years, being sick for six or eight weeks with each attack, and later had two milder rheumatic attacks. He never had syphilis, but had gonorrhea twice as a young man. At the age of 30 he was told that his heart was affected, but he had no symptoms and considered himself in excellent health until the age of 50. From then until the time of his death he suffered from dyspnea and anginal pain on exertion, and because of these symptoms he entered the New York Hospital eleven times, attended the out-patient department regularly, and on two occasions was admitted to Roosevelt Hospital.

His first admission to the hospital was in November 1908, when he complained of precordial pain and tenderness brought on by exertion. At this time he had a transient auricular fibrillation and fairly well marked sclerosis of his peripheral arteries. The heart was somewhat enlarged and there were systolic murmurs at the apex and aortic area, and at times a diastolic murmur heard to the left of the sternum. He remained in the hospital for six weeks. His next admission was in December 1914, when he complained of severe precordial pain brought on by exertion and radiating down the left arm. Blood pressure was not elevated, arteriosclerosis was marked, and the auricular fibrillation had become permanent. He was re-admitted in 1916, 1917, 1918, 1919, 1920, 1921, 1924, and in March and November 1926, each time with the same complaints. On one admission he had a pulmonary embolus and on another an attack of jaundice. In November 1920 he was in the Neurological Institute because of a cerebral accident resulting in right hemiplegia, from which he made an almost complete recovery. In December 1926, while in the hospital, the patient had a sharp chill followed by fever and associated with transient hematuria. Chills and fever recurred daily; no local evidence of infection could be found, but a staphylococcus aureus was recovered from the blood stream; the patient grew progressively worse and died after two weeks. Permission for autopsy was not obtained.

The physical signs changed little in the last twelve years of the patient's life. The blood pressure was never elevated; the heart was somewhat enlarged, with the apex in the 5th space 10.5 cm. to the left of the midline. The rhythm was totally irregular. Systolic murmurs were present at the apex and the aortic area, and at times a soft diastolic murmur was heard to the left of the sternum in the 2nd, 3rd

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or 4th space. Retinal and peripheral arteries showed evidence of sclerosis. The Wassermann reaction was negative on repeated examinations. The electrocardiogram showed auricular fibrillation with left axis deviation and no abnormality of the ventricular waves. The records were practically identical over a period of ten years, a finding which was considered unlikely in the presence of any progressive disease of the coronary arteries.

On each admission to the hospital, and indeed on each visit to the clinic, the patient's complaint was the same. On exertion he became short of breath and had severe pain and pressure under the sternum, in the left side of the chest, radiating down the left arm and up into the left side of the neck. In 1914 the pain radiated to the jaw and left side of the face over the eye and was accompanied by a sense of pulsation in the left temporal region. Generalized sweating accompanied the more severe attacks of pain. In 1918 pain in the throat and hoarseness were noted with the pain. In 1921 the attacks were more frequent and were often followed by pain behind the left ear. Until 1926 the pain was always brought on by effort and relieved by rest; it started under the sternum, spread over the left side of the chest, radiated to the left arm and left side of the neck, and was commonly associated with hyperaesthesia of the skin. In March 1926 the patient stated that he had had several attacks of pain at night, and on admission to the hospital the whole precordial area was sensitive to light touch. On March 29 the following note was made: "Last night patient had a very profuse localized sweat limited to the area where anginal pain occurs,—i.e. precordium, left shoulder and left arm. He has had similar experience two or three times before coming to hospital. Sweat occurs at night and is not accompanied by pain." At this time the pupils were equal and there was no flushing or other vasomotor disturbance. After six weeks of rest the patient went home and was fairly comfortable for six months, but in November he re-entered the hospital for the last time. On December 2 the following note was made: "About once in 24 hours, while sleeping and usually at night, patient complains of profuse sweating of the left side of chest, left arm and left side of neck. It corresponds to the same area where he has previously complained of anginal pain. He rarely has pain with the sweating." There was no change in the signs at this time, but a few days later the patient developed the acute infection from which he died.

COMMENT

A case is reported in which localized sweating occurred, apparently as a substitute for anginal pain. The sweating was limited to the region where the pain had previously been felt and was observed repeatedly in the last year of the patient's life. It was not accompanied by exophthalmos, dilatation of the pupil or other evidence of sympathetic involvement. Cardiac pain was present for the last twenty-five years of the patient's life and was believed to be related to an old rheumatic valvular disease. The patient had generalized arteriosclerosis but no evidence of progressive coronary disease.

PERMANENT BRADYCARDIA FOLLOWING DIPHTHERIA, CASE REPORT*

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THE occurrence of heart-block is well known in severe cases of diphtheria. The development of this arrhythmia is of serious import and often is followed by the death of the patient. In the experience of an authority[1] on diphtheria, the patients who survive the onset of heart-block for a week have a good chance to recover, and in this type of case deaths never occur after two weeks. In the majority of cases, if the patient survive the acute attack, the heart after a few months is perfectly normal even to electrocardiographic examination.

There are but few reports in the literature of the occurrence of a permanent arrhythmia resulting from diphtheria. There is one report of permanent auricular fibrillation,[2] following heart-block; and two of complete heart-block which remained permanent in spite of the recovery of the patient from the diphtheria. The first[3] was a woman of twenty-three years in whom the diphtheria occurred nineteen years previously; the second,[4] also a woman, aged forty-eight, had survived the diphtheria forty-two years. To these I wish to add the report of a case of permanent bradycardia.

CASE REPORT

An American schoolgirl, aged ten years.

Past History.—Had measles, whooping cough and German measles. At the age of 4 years while living in Japan she suffered an attack of "Japanese jaundice." Nausea was the chief symptom, and she was able to eat little for one week. The jaundice persisted from two to three weeks; recovery was apparently complete.

At the age of five years, and after her return to the United States, she contracted a severe attack of diphtheria, which confined her to bed for two and one-half months. Sixty thousand units of antitoxin were administered, the first dose being given on the second day of the illness. There were many complications. Her parents stated definitely that the rate of their daughter's heartbeat suddenly dropped on the seventh day of the diphtheria and the rate has remained slow ever since. There was a "dragging of the legs" following the diphtheria and this rapidly disappeared during the first six weeks of her convalescence, about four months after the onset of the diphtheria. One year later a pediatrician in Chicago noted a slow heart rate, which he believed would gradually disappear, and no other abnormalities.

She never had any form of rheumatism, or chorea, or tonsillitis save at the time of the diphtheria.

Present Illness.—She appeared well and strong subsequent to recovery from the diphtheria. One week ago, however, after running about a half mile she collapsed

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and appeared to be unconscious for a period of about three minutes, and then rapidly recovered. She slept for the next hour. There were no other attacks. She was a very active child and played normally with other children. She was examined by Dr. H. C. Petterson, who noted the bradycardia and referred her for study.

Physical Examination.—A well-developed girl. The heart appeared normal in size. There was a soft systolic murmur with the first sound over the midprecordia.

Fig. 1.—Sections of Lead II taken March 9, 1929. Above: ventricular rate 48; definite P-waves are present and show a progression from a position following to one preceding the QRS complex. Below: ventricular rate 46-50; the P-waves are less constant in form; they are absent after the initial three ventricular complexes; toward the end of this strip coupling occurs; the premature beats are preceded by inverted P-waves.

Fig. 2.—Sections of Lead II taken July 9, 1929. Top: ventricular rate 32; there are traces of what may be a P-wave at a rate of about 110. Middle: after exercise; ventricular rate 39; a trace of a P-wave occurs 0.12 second before each QRS complex. Bottom: after exercise; ventricular rate 52; coupled rhythm is present; the second beat of each pair is preceded by an inverted P-wave.

The heart rate was 48, and after rising from the horizontal to the sitting position six times the rate was 42 per minute. There were periods when the beats occurred in pairs, as in coupled rhythm, and occasionally there appeared to be a single extrasystole. The remainder of the cardiac and general physical examination was normal.

Subsequent History.—There have been no further attacks of syncope. She leads a normal life, but has been advised to avoid strenuous exertion such as the long run.

Electrocardiograms.—Electrocardiograms were obtained at the time of first examination on March 9, 1929, and on July 9, 1929. At the latter date records were obtained at rest and after exercise, such as sitting up and lying down and hopping on one foot.

Selections from the electrocardiograms are given in the accompanying illustrations. The interpretation of these electrocardiograms is not obvious. The tracing obtained on March 9 contains a definite P-wave which might be thought to indicate an impulse from the sino-auricular node, but its evident time relationship to the ventricular complex at such a slow rate and its position sometimes subsequent to the QRS make it more likely that the impulses start from the A-V node. The top strip of Fig. 2 depicts a rate of but 32 which is consistent with idioventricular rhythm; the rate is somewhat higher in the other two and it is probable that the impulses are initiated at a higher level, as in the A-V node. The sole strip which suggests complete dissociation, in case the minute waves are considered to be P-waves, is the top record of Fig. 2. The almost complete disappearance of the P-waves in the electrocardiogram of July 9 is noteworthy.

Study of the entire electrocardiograms obtained on these two occasions warrants the conclusion that there is little if any activity of the sinus node. Exercise in the laboratory failed to accelerate the ventricular rate above about 50 per minute; this result agrees with the clinical observations of the effect of exercise, of both Dr. Petterson and myself.

DISCUSSION

I have both examined and taken an electrocardiogram of the patient reported by Drs. White and Jones and at the time was inclined to doubt the explanation of the complete heart-block as due to diphtheria. It is well known that heart-block may be congenital or acquired and of unknown etiology.[5] However, knowledge of the additional case reported by Read[4] and observation of the case described herein makes me ready to accept all three as due to diphtheria. The history in this last patient is convincingly definite.

The case now reported differs from the others in that there is little evidence of activity of the sinus node; the electrocardiograms of the two adult patients show typical examples of complete heart-block with the auricles beating at a higher rate than that of the ventricles. In my patient the impulses appear to emanate from varying levels of the A-V tissues.

It is also noteworthy that the exercise tolerance was essentially normal in all three patients. The attack of syncope occurring in the little girl after running the half mile may have been due to the Adams-Stokes syndrome. Such explanation appears the more probable from the electrocardiographic evidence of the shifting of the impulse center up and down the junctional tissues, which may be inferred to be damaged by the attack of diphtheria.

It has already been stated that if the patient survives the acute attack of diphtheria, the heart eventually becomes normal both to clinical and electrocardiographic examination. That there are occasional

exceptions to this is suggested by the case now reported and the few cited from the literature. A quotation from one of the most exhaustive studies of the pathology of diphtheria offers support to this opinion. Referring to the heart, Councilman[6] *et al.* state: "Acute interstitial lesions of two sorts are found. In one there are focal collections of plasma and lymphoid cells in the tissue, which may be accompanied by degeneration of the myocardium, but are not dependent upon it. This condition is analogous to acute interstitial nephritis. In the other condition, the interstitial lesion consists of a proliferation of the cells of the tissue and is secondary to the degeneration of the muscle. It is probable that this may lead to extensive formation of connective tissue and some of the cases of fibrous myocarditis may be due to this."

SUMMARY

The occurrence of permanent arrhythmias of the heart is rare after recovery from diphtheria. A case is reported of permanent bradycardia appearing during the course of a severe attack of diphtheria. Electrocardiograms disclosed the impulse center to be the A-V node and junctional tissues, with a shifting of the pacemaker between these locations. As far as I am aware, there are reports of but two other cases similar to the one herein reported, and the latter stands alone in certain respects.

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Department of Reviews and Abstracts

Selected Abstracts

Schwartz, Sidney P., and Schwedel, John B.: Digitalis Studies on Children with Heart Disease. II. The Effects of Digitalis on the Sinus Rate of Children with Rheumatic Fever and Chronic Valvular Heart Disease. Am. J. Dis. Child. 39: 298, 1930.

The purpose of this study was to determine the effects of digitalis on the sinus rate of children with rheumatic heart disease and signs of heart failure and to point out the relationship between the slowing of the sinus rate when present and the relief from symptoms.

Tincture of digitalis was administered in daily doses of 3 c.c. to 12 such children until the appearance of nausea and vomiting. A progressive slowing of the sinus rate was noted in all 7 children who were kept in bed after they had received from 3 to 9 c.c. of the drug during the inactive phase of the disease.

Nausea and vomiting developed in all children as a very late manifestation of digitalis action, after the use of from 24 to 50 c.c. of the drug; whereas slowing of the sinus rate was a very early effect which appeared progressively from the first day. Furthermore sinus bradycardia the only type of slowing of the heart rate which could be considered of therapeutic value was a transitory phenomenon in all children never lasting more than four to seven days at the most. A further reduction in the heart rate was due to heart block.

The authors believe that since there is no quantitative relationship between sinus bradycardia and the appearance of nausea and vomiting the latter cannot be used as a criterion in estimating the optimal therapeutic dose of digitalis for children with chronic rheumatic valvular heart disease.

Schwartz, Sidney P.: Digitalis Studies on Children with Heart Disease. III. Auricular Fibrillation in Children with an Early Toxic Digitalis Manifestation. Am. J. Dis. Child. 39: 549, 1930.

Two children are reported to whom digitalis was administered during an active bout of rheumatic fever because of several signs of heart failure, such as enlargement of the liver and swelling of the face with ascites.

In one child, aged six and one-half years, the daily administration of 3 c.c. of the tincture of digitalis resulted in a progressive increase of the P-R interval with dropped beats and the development of auricular fibrillation after a total of 24 c.c. of the drug had been given within eight days. Nausea and vomiting did not appear until the development of the fibrillation. Death resulted seven hours after the establishment of the arrhythmia. In another child, aged eight and one-half years, auricular fibrillation, with a slow ventricular rate and alternate premature beats of the ventricles, developed after 32 c.c. of the tincture had been administered within nine days. The fibrillation appeared before the premature ventricular beats and disappeared within six days.

In both instances, the development of the fibrillation was considered the result of vagal stimulation by the drug during a period of active carditis.

Because of the dangers involved in the administration of digitalis during active carditis, it is concluded that digitalis is contraindicated in such children with rheumatic fever and signs of cardiac insufficiency.

Whitten, Merritt B.: A Comparison of the Blood Supply of the Right and Left Ventricles in Childhood. Arch. Int. Med. 45: 46, 1930.

By means of celluloid injection and corrosion specimens of the heart, the author has studied the distribution of the blood vessels to the ventricles of the heart in a series of specimens from children.

It was found that at birth and during the latter part of fetal life the right and left ventricles are about equal in vascularity. By the end of the second year the left ventricle has become definitely more vascular than the right. This preponderance increases until about the tenth year of life, after which no increase in the vascular preponderance of the left ventricle could be demonstrated. There is definite preponderance of the venous circulation in the left ventricle as compared with that of the right.

Whitten, Merritt B.: The Relation of the Distribution and Structure of the Coronary Arteries to Myocardial Infarction. Arch. Int. Med. 45: 383, 1930.

By means of injection and corrosion specimens of the heart, the author has studied the relation of the coronary vessels in thrombosis and myocardial infarction. Approximately 40 hearts have been injected and studied. The deep branches of the arteries of the left ventricle leave at right angles and pass directly through the myocardium. The branches of the arteries of the right ventricle spread out in practically the same plane as the larger artery from which they arise. The fact that the injury in infarction is almost always to the left ventricle, whereas the right ventricle rarely is involved seems to depend on the differences in the anatomic structure of the arteries of the two ventricles.

The author believes that the branches that leave the surface vessels at right angles to penetrate the myocardium appear to immobilize the main arteries. This immobilization or anchoring of the main vessels appears to augment its tortuosities possibly leading to kinking or constriction with consequent diminution of its lumen at the point of narrowing.

The author has found that besides the relative absence of anchoring by deep branches the right coronary artery as it swings around the right side of the heart, describes an almost complete semicircle. He believes that this is a protection to this part of the right coronary artery.

Infarction in the posterior surfaces of the left ventricle is much more common than has been heretofore recognized. Infarction at the apex may be due occasionally to occlusion of the right coronary artery.

Infarction in the right ventricle was found only in connection with massive infarction and usually was minimal in amount. The right ventricle although it appears to be less vascular than the left it is not believed to be especially predisposed to failure with age. In fact, the left ventricle is found to be the one to fail most frequently from arterial insufficiency.

Conner, Lewis A.: The Psychic Factor in Cardiac Disorders. J. A. M. A. 94: 447, 1930.

In approaching the subject of the psychic factor in cardiac disorders the author considers this factor first in relation to cardiac neuroses and later in connection with organic disease of the heart. He believes that the psychogenic stimulus arises either from an unfortunate statement of some physician or life insurance examiner; from the occurrence of some dramatic case of heart disease perhaps with sudden death, among the relatives or friends of the patient; from the appearance of some symptom which calls the attention of the patient to his heart and leads to a doubt as to its integrity; or from some profound and pro-

tracted emotional disturbance such as deep grief or prolonged anxiety in which, however, there is at first no element of doubt concerning the state of the heart. He believes that this group of patients represents a most important type of individual requiring special care and handling. Such management of these patients with cardiac neuroses belongs essentially to the realm of psychotherapy. The details of such treatment will, of course, vary with the character of the individual patient and with the predilections of the physician.

The second group is of patients in whom the psychic factor originates in those with organic heart disease. The physician is called on to exercise great discrimination and judgment in differentiating between the symptoms which are the legitimate result of the existing organic disease and those which are merely the expression of the associated psychic upheavals. The physician must know from experience just what is to be expected in the way of symptoms from the type and grade of the organic lesions present.

In discussing the treatment of these patients, the author believes that prophylaxis is of very great importance. Exercise, the occasional use of drugs, the advisability of rest in bed, baths and massage are all discussed.

Wenckebach, K. F.: The Use of Foxglove at the Bedside. Brit. M. J. No. 1, 181, 1930.

In this address the author discusses the use of digitalis at the bedside without instrumental observation. Briefly he states that digitalis is indicated in all cases of heart failure, that is, where insufficient functioning of the heart is the cause of the pathological condition. This holds good irrespective of the cause of the heart failure itself. He follows the old custom of using large, medium and small doses, a distinction which needs no special explanation and is easily followed at the bedside. The only requirement is to adopt a certain unit of activity which may be the basis of this dosage. The author is strongly in favor of the use of dried leaves of digitalis by mouth.

As adjuvants in digitalis treatment the author discusses the use of caffeine and caffeine diuretics. He also believes that the new mercury preparations novasurol and salyrgan at the right moment and in the proper dosage constitutes perhaps the greatest recent progress in the treatment of heart patients. The resulting depletion of the body relieves the overfilled circulation, lessens the circulatory resistance and frees the heart and kidneys from a great part of their task so that it smooths the way for better action by the foxglove.

Diet and venesection are mentioned.

As adjuvants in regulating the heart rhythm the author discusses both strychnine and quinine. He believes that a combination of strychnine and quinine is followed by immediate and lasting success in cases of extrasystolic irregularities without marked heart failure. He cites the instance of a friend with aortic incompetence extremely miserable during the periods of extrasystolic beats who was relieved by strychnine and quinine.

In discussing prolonged digitalis administration he discusses the use of very small doses and larger doses.

Josef, V. Boros: Changes in the Electrocardiogram Following Transient Changes in Conduction. Wien. Arch. f. innere med. **19:** 339, 1929.

This article is a report of two cases showing transient changes in the electrocardiogram. The first case is a fifteen-year-old school boy who in the course of an acute infection showed partial heart block and Wenckebach's periods. The ventricular complexes resembled those usually seen in right axis deviation; that is, low S waves in Lead I, and inverted T-waves in Leads II and III. The fol-

lowing day he had completely recovered. The A-V conduction time was now normal and the ventricular complexes now had diphasic T waves in Lead II, and positive T-waves in Lead III. Later still the ventricular complexes became completely normal. The author interpreted these changes as being transient disturbances of intra-ventricular conduction.

The second case was a sixty-two-year-old man with degenerative heart disease and congestive heart failure. He showed two to one heart block with an auricular rate of 160 and a typical P-wave. As he recovered, his auricular rate slowed down and his heart block disappeared. He now showed normal upright P-waves with increased conduction time (0.30 seconds). The author interprets this return to normal as a result of improved conduction through the auricles, while the auricular rate was slowed.

Fahr, Th.: Contribution to the Question of Rheumatic Granulomatosis. Klin. Wchnschr. **8:** 1995, 1929.

This is a discussion based on a case description and refers to the fact that rheumatic nodules may be found both in the pericardium and in the tonsils, and in the tissues surrounding the joints.

The author is of the opinion that these lesions are as specific as those of tuberculosis or Hodgkin's disease and therefore suggests the name Rheumatic Granulomatosis for the disease which we have hitherto known as rheumatic fever. He discusses the pathogenesis of the disorder and believes that the streptococcal element of both rheumatic fever and of scarlet fever is superimposed upon the original condition, the nature of which is ill understood, but which probably is allergic in origin. He emphasizes that rheumatic fever may be found without Streptococcus viridans and that the organism may be found in persons who have no other evidence of rheumatic infection.

Ionescu, Von Prof., and Railcanu, C.: Experimental Investigations on the State of the Cardiac Muscle after Extirpation of the Stellate Ganglion. Wien. Arch. f. inn. med. **19:** 199, 1929.

The author removed the stellate ganglion on one or both sides of the neck of rabbits and dogs. The animals recovered completely from the operation and in their behavior showed no difference from healthy animals with whom they were running about. The operation produced no change in the microscopical section of the heart muscle.

Thirty to 380 days after the operation, the sections showed no histological changes neither of inflammatory nor of degenerative nature. Nor were any histological changes observed in the periaortic or pericardiac ganglia.

Palmer, Robert Sterling: The Significance of Essential Hypertension in Young Male Adults. J. A. M. A. **94:** 694, 1930.

The author reports that in 3598 records of physical examinations done from the department of hygiene of Harvard University it was found that slightly more than 10 per cent of those examined showed systolic blood pressure about 140 mm. of mercury and 2.25 per cent of the whole group showed systolic pressures of 150 or more without other abnormalities. The urine examination in all instances was negative. The systolic pressures were all more than 10 per cent above the level expected when height, weight and age were taken into consideration. Approximately half of these individuals showed diastolic pressures more than 10 per cent above the calculated normal while only one-fourth of a normal control group showed an elevation in the diastolic pressure. A large proportion of nervous and neurotic types was found among those showing systolic pressures

above 140 and among those showing pressures between this level. There was no correlation between the infectious diseases or constipation and hypertension in this series as compared with a normal series of equal size.

One hundred and fifteen persons, 66 from the normal control series and 49 from those showing hypertension were followed over an interval of ten years. Of the 66 normal individuals, 3 or 4.54 per cent had systolic pressures over 140 and one had a systolic pressure of 150. Of 49 subjects who showed pressures over 140 at the first examination, 12.2 per cent showed systolic pressures between 140 and 150 after ten years and 10.2 per cent showed systolic pressures of 150 or over, the highest being 180. Thus if hypertension is found at twenty years of age it is somewhat more likely to be found persistent after ten years than it is to develop during this interval.

Those showing hypertension at the original examination ten years or more earlier when followed give a history of vasomotor symptoms in one-fourth of the cases as compared with such a history in one-seventh followed from the normal group.

The incidence of cardiovascular disease in the family histories of a normal control and the hypertensive groups was approximately the same.

White, Paul D., and Churchill, Edward D.: The Relief of Obstruction to the Circulation in a Case of Chronic Constrictive Pericarditis. New Eng. J. Med. 202: 165, 1930.

A review of the condition of the heart and pericardial sac in chronic adhesive pericarditis together with the progress of the patient leading up to the signs and symptoms of cardiac embarrassment is presented and discussed. Various types of operations that have been devised for the relief of this cardiac embarrassment are briefly described.

A case herein reported is of particular interest because of the striking benefit that resulted during the year following the operation of pericardial decortication. The operation performed was as follows: five costal cartilages from the third to the seventh inclusive were resected with short portions of the fourth and fifth ribs. Through this approach with the left pleura retracted laterally, the pericardium was exposed. It was found to be much thickened and scarred and it firmly enclosed the heart which was obviously unable to pulsate freely in its grip. A sheet of pericardium about the size of the palm of the hand was resected from the anterior aspect of the heart. At once the heart expanded through this gap in the rigid pericardial membrane and its pulsations obviously increased in extent and freedom. The left side of the sternum was cut away with rongeurs and the dissection of the pericardium was continued a short distance further as far as the right auricle. Finally a constricting band with calcareous nodules kinking the inferior vena cava just above the diaphragm was discovered and resected allowing the great vein to resume its normal calibre. At the end of the operation the muscle and skin flaps were brought back into position over the exposed heart.

During the past year since the operation, the patient has continued her steady improvement so that now she lives a perfectly normal life for a girl of her age, nineteen years. She has been able to walk several miles a day, to dance, and even to run for trains without undue shortness of breath. The etiology of the pericarditis in this case is unknown.

Tallerman, Kenneth H., and Jupe, Montague H.: Displacement of the Heart in Pneumonia in Childhood. Arch. Dis. Child. 4: 230, 1929.

Five cases are described in which during an attack of pneumonia the heart deviated toward the side of the lesion subsequently returning slowly to a normal

position as recovery occurred. A consideration of these cases and of other similar cases reported in the literature points to the fact that this phenomenon is not infrequent in childhood and would in all probability be more often noted if specially looked for by physical examination and if radiograms of the chest were taken early. Displacement of the heart appears to be brought about by the traction exercised by shrinkage due to partial collapse of the affected lung, aided by the push of the sound lung which is frequently distended by compensatory emphysema.

This cardiac displacement is not caused by a pulling over due to fibrosis, since it occurs in the acute stage of the disease and the heart subsequently returns to its normal position. Moreover, neither by physical nor by radiological examination can evidence of fibrosis be noted.

McLean, C. C.: Early Rheumatic Infections of Childhood. Arch. Ped. 46: 657, 1929.

The author reports 118 cases of early rheumatic infection seen in private practice in Birmingham, Alabama, during the past eight years. There were 51 boys and 67 girls included in the study. The age of greatest frequency was from five to eight years. The most common symptoms presented by the patients when first seen were poor appetite, failure to gain weight, nervousness, fatigue, repeated attacks of tonsillitis and nasopharyngeal infection, and pain in the legs, joints or stiffness of limbs. Forty-four children had tonsils and adenoids removed when the diagnosis of rheumatic infection was made but most of these cases gave a history of repeated attacks of tonsillitis and suggestive symptoms of a rheumatic infection before the operation. There were signs and symptoms of mild chorea in 42 of the children. Of the 118 cases 84, or 71 per cent, had soft blowing systolic murmurs. These murmurs were heard in 52.3 per cent of the chorea patients and in 81.5 per cent of the 76 who had no signs of chorea. Apparently there was little or no hypertrophy of the heart.

Of the 118 children there were 103 underweight for their height. There were 35 of the 118 cases who developed symptoms and physical signs of rheumatic infection while under observation. Many of these children were original feeding cases who had been under care throughout their lives. There were 92 cases in which the foci of infection was thought to have been located in tonsils, teeth, sinuses, ears, or nasopharyngeal tissue.

The author describes in brief the management instituted in the care of each of these children. He stresses rest in bed and removal of foci of infection. Several case reports are included.

In conclusion, he believes that every child with manifestations of an early rheumatic infection is a potential cardiac patient and should be managed accordingly.

Coates, Vincent: The Relation of Orthodox Rheumatic Infection to Multiple Infective Arthritis. Brit. M. J. 1: 67, 1930.

By orthodox rheumatic infection the author means frank rheumatic fever and by multiple infective arthritis he means that type of subacute or chronic arthritis which is nonsuppurative and is due to an infection of a nonspecific character.

He has studied the possible relationship between these two conditions by the following methods:

1. The evidence afforded by the family history of fifty consecutive cases of multiple infective arthritis in regard to orthodox rheumatic infection. In 16 instances rheumatic fever was known to have occurred in a parent, brother or

sister. He believes that this incidence of 32 per cent accords with the popular conception that "rheumatism" has a familial or hereditary basis.

2. The incidence of a clear history of orthodox rheumatic infection in 300 consecutive cases of multiple infective arthritis. Rheumatic fever is believed to have occurred in 14 instances.

3. The occurrence in the aforesaid 300 cases of cardinal signs of orthodox rheumatic infection, namely, cardiac lesions and subcutaneous nodules. In the 300 cases 4 per cent showed cardiac lesions and 6 per cent subcutaneous nodules.

Rothman, Phillip E.: Digitalis Therapy. Its Use in Children. California & West. Med. 30: 150, 1929.

The author discusses briefly and completely the indications, methods of administration, and signs of digitalization in children. He believes that children apparently fall into the category of individuals whose vagus centers are more easily stimulated than usual or whose hearts are unusually susceptible to the slowing action of the vagus. He believes that there is a tremendous individual variation in the tolerance of children that makes a detailed examination of the patient an absolute necessity before the administration of the next dose.

Herrick, James B.: Atypical Features of Acute Coronary Occlusion. Ann. Int. Med. 3: 105, 1929.

The picture of acute coronary occlusion must not be drawn with too fixed lines. Allowance must be made for many variations from the ordinary type, for mild and subacute cases, for cases without pain, for instances of extreme variation in blood pressure, degree of dyspnea, temperature, pulse rate and rhythm. One must see as well cases with early or late embolic accidents, for recurrence due to proximal increase in the thrombus or to involvement of new vessels. If all this is done, the condition will be recognized more frequently even than now and probably a larger percentage of deaths from angina pectoris will be shown to be due to this accident in the coronary artery.

Coombs, Carey F.: The Diagnosis and Treatment of Rheumatic Heart Disease in Its Early Stages. Brit. M. J. 1: 227, 1930.

In this British Medical Association Lecture, the author discusses many of the features of rheumatic heart disease in children particularly in a group of 653 children with rheumatic heart disease seen in a cardiac clinic. He believes that progress in the treatment of these children depends on the same principles as those involved in the fight against all infections, *early* diagnosis and *persevering* treatment. If rheumatic injury to the heart is to be recognized in an early stage, it can only be done by remembering that symptoms of cardiac insufficiency do not appear till the lesions are already established and severe.

He believes there are four different approaches to a diagnosis of cardiac rheumatism in its early stages.

1. The easiest of these is that in which the rheumatic infection declares its presence within the body by provoking either arthritic pains or chorea. He believes that pain persisting more than a day or pain which makes the child lame ought to be noticed, also that if the child looks ill or has a rise of temperature, however small, with pain a physician should be seen. He believes that every child who has rheumatic polyarthritis that can be recognized as such may be assumed to have an infected heart also even if there are neither symptoms nor signs of this.

2. Rheumatic carditis is so often preceded by an attack of tonsillitis that one ought to consider repeated examination of the heart an essential part of the care of any child with inflamed tonsils. He believes that children convalescent from tonsillitis ought to be seen a few days after every obvious symptom has cleared up.

3. The most important of all these methods of securing an early diagnosis of cardiac rheumatism is that which it is hardest to practice and easiest to forget; the fact that the heart may become definitely and permanently damaged by rheumatic infection without any other perceptible manifestation of the infection. Of 1100 children referred to the cardiac clinic by the School Medical Service for an opinion on the state of the heart, 653 have been judged to be suffering from rheumatic heart disease. During the same period in the same city, 238 cases of heart disease have been reported from private practice of medical men. It seems, therefore, as if for every case of rheumatic carditis that makes itself known to a medical man at the time when it is established, there are two that are not found until the child is examined as a part of the school routine. In order to recognize such cases early, the author believes that early symptoms of heart disease are not cardiac but constitutional; loss of appetite, vague "seediness," increased pallor and above all loss of weight.

4. Finally there are a few children in whom the first symptoms point to heart disease. These children fall into two groups. First, those who are taken with an acute febrile illness with chest symptoms. Second, another group who are brought in because of breathlessness. This is a very small group, because it takes a severe degree of cardiac disease to make a child visibly breathless. Whether the carditis is acute or chronic, it must be severe if it is to produce symptoms of cardiac insufficiency.

The author devotes considerable time to a discussion of cardiac arrhythmias and murmurs made out in these children. He discusses the mistakes that may be made in paying too much attention to these signs alone.

Finally, he discusses the treatment of these children. This may be summed up chiefly in providing complete rest in bed at home or in convalescent institutions. He discusses briefly the use of salicylates.

Miller, Reginald: The Diagnosis of Early Juvenile Rheumatism. Brit. M. J. 1: 230, 1930.

The author discusses the symptoms and signs of early juvenile rheumatism under four main headings. He doubts the existence of a rheumatic diathesis and believes that rheumatism in these children is an environmental disease. He also has no liking for the term "prerheumatic child." He believes that a prerheumatic child is the ordinary rheumatic child who has not yet suffered a knock-out attack of the infection.

The first group of symptoms discussed are those of a constitutional nature. He believes that rheumatism is the result of a generalized systemic infection and that the child is inclined to show a general ill health. Such a child is pale, sallow, unhealthy in appearance, poor appetite, irritable nerves, poor sleep, occasional cough and shortness of breath. The child's most important symptom usually is fatigue. He discusses the similarity of these symptoms to a tuberculous infection.

The second group is the most easily recognizable group of children with sore throats and pain in the joints. He discusses the relationship of infected tonsils to these children, particularly the advisability of tonsillectomy.

The third group shows symptoms referable to nervous instability and actual chorea. He is inclined to believe that a rheumatic child becomes nervous even though actual chorea is not present.

The fourth group is made up of children who show signs in the heart indicating rheumatic infection. The signs most suspicious of rheumatic heart disease are as follows: (a) increased pulse rate, (b) dilatation of the left ventricle, (c) the presence of an apical systolic murmur with enlargement of the left ventricle, (d) presence of a reduplicated apical second sound or of a mid-diastolic apical murmur.

Wedd, A. M. and Hubbard, R. S.: Notes on Dosage and Excretion of Quinidine Sulphate. Clifton Med. Bull. 15: 69, 1929.

The authors have made qualitative tests of the excretion of alkaloid in the urine of a number of patients suffering from paroxysmal disorders of the cardiac mechanism who were receiving either quinidine sulphate or quinine hydrobromide in small doses over a period of several weeks. The test applied was precipitation of quinidine sulphate and quinine hydrobromide in distilled water and in urine by potassium mercuric iodide solution (Mayer's reagent).

In the present series of patients when 0.2 gram of quinidine sulphate was given, the alkaloid appeared in the urine within three hours and faint traces were always found at the end of twelve hours. In one patient, the urine showed a faintly positive reaction after twenty-three hours. An interesting exception occurred in a man suffering from advanced renal insufficiency; the blood urea nitrogen was 52 grams; there was no demonstrable passive congestion or edema; after 0.2 gram of quinidine sulphate was given, there was none in the urine obtained four hours later and the night urine was only faintly positive for the alkaloid; the urine at 9 o'clock the next morning was negative for alkaloid even in acid solution.

When patients were given 0.6 gram of quinidine sulphate or one gram of quinine hydrobromide daily in three doses all specimens of urine showed the presence of alkaloid. Certain patients suffering from paroxysmal auricular fibrillation have been helped by such quantities of these drugs but the presence of alkaloid in the urine bore no relation to therapeutic effects. Quinidine excretion is doubtless influenced by a number of factors, individual variation, diuresis, renal permeability for substances other than water and muscular effort.

Kissane, R. W.: Area of the Body Surface and Measurements of the Normal Heart in Children. Arch. Int. Med. 45: 241, 1930.

In a previous report the necessity of finding a variable that has a close correlation with the size of the heart was emphasized and the area of the body surface was suggested because it includes other variables such as height, weight, age, sex, and diameter of the chest when persons of ideal weight are used as a standard. The present paper reports the determination of the size of the heart for an area of body surface of less than 1.5 square meters, 100 children between the ages of three and fourteen years with normal hearts and electrocardiograms being measured.

Height and weight without clothing were obtained in each case. Roentgenograms were made at a distance of six feet and measured for the transverse diameter of the heart and the diameter of the chest. The cases were classified as to their relation to ideal weight for a given height and age, the table of Woodbury being used for subjects under five years of age and the table of Baldwin and Wood for those above this age. For the determination of the area of body surface, the table of Benedict and Talbot gave the best results.

The author believes that cases of ideal weight for height should be used in the estimation of the measurements of normal hearts since cases of over or under

ideal weight for height have an antagonistic influence on the close correlation of the area of body surface with the mean transverse diameter of the heart.

In this series of children the mean transverse diameter of the hearts in girls was smaller than that in boys at any age. The area of body surface has the same close correlation to the size of the heart in children as in adults.

Increase in the weight of children as a group increases the range from the mean transverse diameter of the heart with the area of body surface as a variable.

Duke, W. W.: Heat and Effort Sensitiveness, Cold Sensitiveness. Arch. Int. Med. 45: 207, 1930.

In this paper the author enumerates a series of relatively common illnesses many of them serious which are caused rather frequently, he believes, by a disorder in the heat regulating mechanism. The illnesses include heat prostration, symptoms of effort syndrome, noninfectious coryza, asthma, urticaria, dermatoses and other miscellaneous ailments to be mentioned. They are commonly diagnosed neurasthenia, psychasthenia, allergy, atopy, vagotonia and eczema. The patients are hypersusceptible to infection during their reaction to heat or cold, especially infection in the nasorespiratory tract and for this reason their disorders are often classed with the infections.

The author discusses our present knowledge concerning the heat regulating mechanism of the body and the relationship of the body to outside temperature conditions and changes. He discusses the manifestations of typical heat and cold sensitiveness and the process of acclimation and declimation. He also discusses the relationship of heat and cold sensitiveness to infection, to atopy and to histamine-like bodies that have been described by Lewis, Eustis and Lewis and Vaughn.

The relationship that rheumatic fever has to climatic conditions and changes has been known for a long time. Many of the ideas discussed in this paper by the author might find some application to the occurrence of rheumatic fever in susceptible individuals. The part played by dampness, by heat and by light in the etiology of rheumatic fever might thus be explained. That rheumatic subjects are suspectible to heat changes and to infection is well known. The idea included in this paper is an important contribution to the present discussion as to the nature and etiology of rheumatic fever.

Levine, Samuel A., Ernstene, A. Carlton, and Jacobson, Bernard M.: The Use of Epinephrine as a Diagnostic Test for Angina Pectoris. With Observations on the Electrocardiographic Changes Following Injections of Epinephrine into Normal Subjects and into Patients with Angina Pectoris. Arch. Int. Med. 45: 191, 1930.

Epinephrine was administered subcutaneously in doses of 1 c.c. to 3 groups of persons: To one, a group of 11 with angina pectoris, a second of 10 of the same average age but without angina and a third of 10 normal young adults. In all but one patient with angina pectoris, typical pain resulted from the injection. In none of the control patients did this pain occur. Electrocardiographic studies showed that following the injection of epinephrine the T-wave in the anginal group increased slightly in amplitude while in the other two groups it showed a tendency to decrease. The increase in blood pressure and pulse rate was somewhat greater in the anginal group than in the others.

It is suggested that the production of anginal pain by the injection of epi-

nephrine may serve as a diagnostic test for angina pectoris. The test would not be applicable when the diagnosis is certain but rather in doubtful cases or when there are other possible explanations for the symptoms, such as gallstones or disease of the stomach or the duodenum.

Because epinephrine produces typical pain with great regularity in patients with *angina pectoris, therapeutic use of the drug in such patients* should be carried out with great caution.

Fullerton, Charles, and Harrop, George A., Jr.: The Cardiac Output in Hyperthyroidism. Bull. Johns Hopkins Hosp. 46: 203, 1930.

The authors have estimated the cardiac output by measuring the rate of absorption of nitrous oxide from the alveolar air into the blood. Eight carefully selected patients with typical manifestations of the disease without evidence of organic cardiac disease or of lung disease were studied. The clinical examination was confirmed by electrocardiographic studies and x-ray examination of the chest. The technic and apparatus were those employed by Marshall and Grollman. The determinations were done upon the patients as soon as possible after admission to the hospital and then at intervals during the course of their treatment. The first point to be noted is that under basal conditions where quiet and relaxation were realized as much as possible the increased pulse pressure usually reported in hyperthyroidism was not found. Surprisingly little difference also was found in the blood pressure before and after treatment even over prolonged periods.

Since the difference in blood pressure before and after treatment is very small, *the difference in cardiac output should then be a direct measure of the increased* cardiac work. They found a parallelism between the increase in the basal metabolism and the cardiac output per minute. They believe that the work of the heart is increased at least to this amount. The fairly close relation which exists between elevation of metabolism and cardiac output in hyperthyroidism strongly suggests that the level of the metabolism in the disease is a factor of the first importance in the regulation of the cardiac output per minute under basal conditions.

Johnson, Charles C.: The Salicylates. XIX. The Question of Acidosis Following the Administration of Salicylates. J. A. M. A. 94: 784, 1930.

The author has studied the effect of administration of readily absorbable salicylates in doses equivalent to full therapeutic doses, on the alkali reserve of the blood in rabbits and cats. He found that the administration of these salicylates caused a definite and general marked respiratory stimulation, though the hydrogen-ion concentration remained unchanged and there was no acetone demonstrable in the urine. These changes are best reconciled as the equivalent of a fixed acid acidosis, compensated by loss of carbon dioxide. Definite increases in blood lactate were correlated with significant decreases in alkali reserve and respiratory stimulation in four of eight cats receiving sodium salicylate in doses equivalent to the full therapeutic; the remaining four cats did not show evidences of acidosis, but in view of the respiratory and blood changes that occurred there was still a correlation between these functions. Various possibilities regarding the origin of the increases in the fixed acid occurring in salicyl medication are indicated.

The author believes that the use of bicarbonate together with salicylates in full therapeutic doses in rheumatic fever and also in the treatment of salicylate poisoning is rational on experimental grounds at least.

Strauss, Maurice B.: Paroxysmal Ventricular Tachycardia. Am. J. Med. Sc. **175:** 337, 1930.

The author reports two cases of paroxysmal ventricular tachycardia and reviews the literature briefly relating to sixty-three cases. No common single etiological factor could be discovered but 84 per cent of the cases occurred in patients suffering from organic heart disease and of these 60 per cent had been treated with digitalis prior to the onset of the tachycardia. In the absence of organic heart disease the prognosis of paroxysmal ventricular tachycardia is good.

The diagnosis at the bedside can usually be made from a slight irregularity frequently noted on auscultation which is found in tachycardia of ventricular origin not to be found in other forms. The quality of the first heart sound may perceptibly vary in different cycles. Vagal stimulation and ocular pressure are never effective in terminating a paroxysm of ventricular tachycardia. Positive diagnosis can only be made by the electrocardiograph.

Quinidin offers a valuable remedy with uniform success in ending the tachycardia.

Keefer, Chester S.: The Beriberi Heart. Arch. Int. Med. **45:** 1, 1930.

A group of 15 patients with beriberi were studied with particular reference to the cardiovascular system. It was clearly demonstrated that patients who developed cardiac insufficiency are those who have the least involvement of the nervous system. The author believes that when the peripheral nervous system becomes involved so as to produce paresis that the heart muscle is protected by the lack of activity to a degree that cardiac insufficiency either does not develop or remains slight. Whereas, if the heart muscle becomes involved first then signs of cardiac insufficiency predominate.

The hypotheses that have been advanced in explanation of the mechanism in heart failure in this disease are reviewed and the mechanism discussed. He believes that the right heart is involved to a very great extent. This can be demonstrated by electrocardiographic and roentgenographic examinations. The process in the heart muscle consists of edema and injury to the contractile heart elements. The deficiency of Vitamine B probably plays an important part in this change. The importance of diet and exercise in the management of this form of heart disease is emphasized.

Werner, Walter I: Tuberculous Pericarditis. Am. Rev. Tuberc. **21:** 202, 1930.

Of 67 tuberculous patients autopsied, 4 or 5.9 per cent had tuberculous pericarditis. The author reports 3 of these cases, two of which were recognized clinically. He points out that the symptoms of tuberculous pericarditis are very obscure and the diagnosis depends upon a general survey of the case with reference to the probability of tuberculous infection. In the acute miliary form, the diagnosis is generally impossible, the pericardial reaction being too slight to attract attention. In the subacute form it may also be overlooked. It is often revealed by special symptoms especially pain and x-ray examination. Occasionally the pericarditis is associated effusion. The fluid may be hemorrhagic or purulent. Tubercle bacilli may be recovered from this fluid.

Wiggers, Carl J.: Studies of Ventricular Fibrillation Caused by Electric Shock. Am. J. Physiol. **92:** 223, 1930.

The author has studied ventricular fibrillation caused by electric shock particularly the question of the revival of the heart from such fibrillation by successful use of potassium and calcium salts. He discusses fully the reported in-

stances of recovery from fibrillation and believes that they occur under conditions unattainable in the intact heart or that the recovery resulted from the use of methods not applicable to the intact heart or that the condition was not proven ventricular fibrillation produced by electric currents.

He points out that it is important to demonstrate that cessation of ventricular activity exists at the time the measures directed toward recovery are instituted. Under these conditions there may be some doubt that revival of the heart itself is possible since fibrillation lasts as a rule from fifteen to fifty minutes, the average duration being twenty-four minutes. Under these conditions anemia of the brain may have existed so long as to make recovery of the whole body impossible.

He believes that potassium-calcium perfusions may be used either by coronary perfusion, by direct injection into the ventricular muscle, or by injection within the ventricular cavity. After the cessation of fibrillation by the use of potassium perfusion a coordinated beat may be restored by similar perfusion of an isotonic solution containing an excess of calcium.

Coronary perfusion demands the sacrifice and ligation of a carotid artery under aseptic conditions, a performance requiring rather elaborate perfusion apparatus and therefore is frequently not adaptable to practical needs. Furthermore, such perfusion is apt to result in a filling up of the dead spaces of the circulation rather than an introduction of the fluid within the ventricular cavity. Injection into the ventricular cavities of the solution causes a resumption of a coordinated beat provided the fluid is pumped through the coronary vessels by massage. Without massage it is ineffective. This is particularly true of the calcium solution. No chemical substitute for massage has been found as a result of extensive experimentation.

The author concludes that while the methods offer some promise of success when applied promptly to patients after electric shock, hope of resuscitation in man by methods so far devised is necessarily limited to cases in which the surgical possibilities and circumstances approximate those obtainable in laboratory animals. The fact that cardiac massage is required is a serious drawback to the practical use of the intracardiac method in the field.

Book Reviews

TRAITÉ D'ELECTROCARDIOGRAPHIE CLINIQUE. By Paul Veil and Juan Codina-Altes. G. Doin et Cie, Paris.

The authors of this work are pupils of Gallavardin, eminent French cardiologist, who has written an excellent preface emphasizing the importance of the electrocardiographic method. Cluzet, Bret, and Bard, all of Lyon, have also contributed; the first, a chapter on the origin of the electrical currents produced by the cardiac muscle; the second, a chapter on cardiac hypertrophy studied by the method of Müller; and the last, a section upon the influence of the intracardiac pressure upon the cardiac mechanism, normal and abnormal. Rothberger of Vienna has given an excellent account of his ideas concerning parasystole.

The scope of the work is similar to that of *The Mechanism of the Heart Beat* by Lewis and *Unregelmässige Herztätigkeit* by Wenckebach and Winterberg. On the whole it is less satisfactory than either of these monographs, although it is an excellent discussion of the subject and presents a different viewpoint. Unfortunately a large proportion of the figures, of which there are a great many, are so poorly reproduced that they are almost, if not entirely, illegible. In a few instances the figures are upside down, and one or two of the legends obviously belong to some figure other than the one which they accompany. One or two figures taken from the works of others are attributed to the wrong source.

The book contains no bibliography. In a few instances specific reference to the work of others is given; usually, however, only the name of the authority whose work or opinion is quoted is given. Consequently it is impossible to find the original contributions which are referred to.

The authors attribute a much greater rôle to the intrinsic cardiac nerves than do most cardiologists in this country. They also show a very pronounced tendency to divide and subdivide the disturbances of the heart beat into a great many clinical syndromes, not all of which are well defined. As an example we may refer to their discussion of paroxysmal tachycardia. They recognize three chief types:

I. *Tachycardies paroxystiques du type Bouveret.* This is the classical form of the disorder. The authors believe that it is not due to a succession of extrasystoles, and that it is in no way related to extrasystolic arrhythmia. They state that when extrasystoles do occur at the beginning or end of an attack, or when they occur between attacks, they are never of the same form as the beats of the paroxysm itself, and consequently do not arise at the same point and are not generated by the same mechanism. They distinguish between long attacks which occur at relatively long intervals, and very short attacks which occur with great frequency. They refer to the latter condition as "Tachycardie paroxystique à centre excitable."

II. *Tachycardies paroxystiques d'origine extrasystolique.* The authors regard this type as entirely different from that described above. It is made up of a succession of extrasystoles. When the attacks are short and numerous; that is, when relatively few extrasystoles occur in succession, each group of extrasystoles being separated from the group which precedes and that which follows it by one or more normal beats, the condition is referred to as "*extrasystoles en salves.*" Very long attacks which they regard as relatively rare are spoken of as "*extrasystoles massées.*"

III. *Tachycardies anormales.* This group is poorly defined; it contains those cases which do not seem to the authors to belong to either of the two previous groups. It is divided into two divisions:

A. Non-terminal. Under this heading a number of examples of tachycardia, no two of which are alike, except that all are benign, are discussed.

B. Terminal. These cases are mostly examples of ventricular tachycardia in which the ventricular complexes varied greatly in form.

The same tendency to recognize a great variety of syndromes is found in the discussion of atrio-ventricular rhythm and of sinus arrhythmia. The authors believe that true atrio-ventricular rhythm is usually irregular. They are particularly interested in those cases in which there is complete atrio-ventricular dissociation, but in which auricles and ventricles are contracting at the same rate, or nearly the same rate, the former responding to the sinus node, the latter to the A-V node. To this condition they give the name "*Dissociation isorhythmique*," of which they distinguish several varieties. A study of this condition as well as other observations have led the authors to believe that the intrinsic cardiac nerves act as a regulatory apparatus which coördinates the various impulse-producing centers of the special tissues. Some disturbances of the heart are regarded as due to disturbances of this coördinating mechanism; others as due to its normal regulating function. They speak, for instance, of non-compensatory arrhythmias; benign extrasystoles, ordinary paroxysmal tachycardia, which are due to hyperexcitability of ectopic centers produced by hyperactivity of the sympathetic nerves. In this case the coördinating mechanism is disturbed. Certain extrasystoles, ventricular escape, certain types of nodal rhythm, certain types of bigeminy, on the other hand, are regarded as compensatory phenomena, due to an attempt on the part of the nervous regulatory mechanism to maintain a normal heart rate. To the reviewer these ideas seem too speculative for general acceptance in the present state of our knowledge.

As regards the form of the electrocardiogram, the authors are much more conservative. They do not believe that the form of the ventricular complex is of any value in the diagnosis of valvular lesions and regard the broad deformed auricular complex of mitral stenosis as the sole change in the form of the electrocardiogram which can be considered at all characteristic of a valvular defect. Their views of the T-deflection, and of curves of small amplitude do not differ materially from those current in America. They regard preponderance curves as the result of intraventricular conduction defects.

F. U. W.

THE CLINICAL ASPECTS OF VENOUS PRESSURE. By J. A. E. Eyster. New York, The Macmillan Company, 1929.

In this small volume Dr. Eyster gives a résumé of the literature and of his own work on the subject of venous pressure. He discusses the mechanics of venous pressure and the relation of increased pressure to the symptoms of cardiac failure, the methods of determining venous pressure and the findings in normal individuals, in patients with cardiac decompensation and in conditions other than cardiac failure. Because increase in venous pressure is an important factor underlying the symptoms of cardiac failure and an index of such failure and because such increase can be determined accurately and easily, the author feels that venous pressure determinations should receive more attention, and in this book he writes especially for the clinician.

E. H.

LES ANÉVRYSMES ARTÉRIO-VEINEUX. By Raymond Grégoire, Professor of the Paris Faculty of Medicine and Surgeon to Tenon Hospital. Baillière, Paris, 1930. Pp. 214 (with 5 plates and 8 figures).

Experimental work and observations made during the War have enlarged our knowledge of arterio-venous aneurysms. Professor Grégoire, by study and experience, is specially qualified to discuss this subject, and in this monograph he emphasizes the pathological physiology and presents his own ideas and technique of operative treatment. He illustrates his text with well-chosen drawings and case reports, and discusses the subject under the headings of causes, pathological anatomy, physical signs and their physiological meaning, prognosis, diagnosis and treatment. The chapters on treatment and on aneurysms in particular locations fill the second half of the book and should be very useful.

E. H.

THE VOLUME OF THE BLOOD AND PLASMA IN HEALTH AND DISEASE. By Leonard G. Rowntree, and George E. Brown with the Technical Assistance of Grace M. Roth. Philadelphia, 1929, W. B. Saunders Company.

This little book is timely and welcome. It presents in condensed form the available knowledge concerning the variations in blood and plasma volume found in normal individuals and in many disease conditions, and represents the accumulated results of a number of years of patient careful work. The need of supplementing our routine blood examinations by some method of measuring the total volume of the blood must long have been felt by every thoughtful clinician, but no such method has yet come into general use. The authors are convinced that the dye method, introduced by Keith, Rowntree and Geraghty fifteen years ago, has stood the test of time and that it is a "practical procedure of great clinical importance." It seems probable that the appearance of this book will do much to popularize the use of the dye method and that it will attract attention to the importance, in any clinical study of the blood, of a variable which hitherto has received much less consideration than it deserves.

L. A. C.

The American Heart Journal

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Original Communications

REMINISCENCES OF THE LATE PROFESSOR WILLEM EINTHOVEN*

A. SAMOJLOFF
KASAN, U.S.S.R.

DR. WHITE asked me if I would tell of my reminiscences of the late Professor Einthoven. I knew, esteemed, and loved this man, and therefore I willingly accepted the invitation. I only regret that insufficient command of English does not allow me to express clearly and plainly all my thoughts and feelings. As you all know, Einthoven worked almost exclusively in the region of electrophysiology. This branch of physiology stood for a long time completely isolated from life, medicine, and even from the general path of the development of physiological knowledge; shut off in this way, electrophysiology could not progress and it seemed that it would be difficult to alter this sad situation of the study of animal electricity.

Among different favorable circumstances I will point out the one which opened at once new possibilities for electrophysiology, namely, the invention by Lippman, a physicist in Paris, of a new instrument, the capillary electrometer. This instrument rapidly proved its usefulness in the study of electrical phenomena in the animal body, especially after Waller showed that the capillary electrometer was able to register not only the action currents of an isolated animal heart, but also the action currents of the heart of an intact animal and even the action currents of the human heart.

In my youth I became interested in electrophysiology, and when I saw for the first time in a microscope the movements of the mercury meniscus produced by the heart, I may say I was conquered by electrophysiology forever. With the modest instruments I had at the time, I tried to record the curves of a capillary electrometer, and I was thrilled when successful.

One day I obtained a copy of Einthoven's article in Pflüger's *Archives* with records of the action currents of a human heart: I

*Presented at the Massachusetts General Hospital, Boston, September, 1929.

understood that my technique was only a feeble attempt at the solution of the problem which in the hands of Einthoven was brought to the state of complete perfection. I spent hours examining these curves, and asked myself: Who is this man, what is he like and by what means does he obtain such results? Such sharpness distinguishing the curves of Einthoven was never attained before. But such curves soon ceased to satisfy Einthoven on account of their inability to give accurately the changes of action with the time. He developed a method of correcting the curves and then I admired not only his technique but also his theoretical knowledge. These two accomplishments showed the essential features of Einthoven's talent. His mind worked like an instrument of precision. He worked only on what could be measured, and his measurements reached the limit of precision possible under the circumstances. Later we all could see that the subjects he chose for his investigations always lent themselves beautifully to precise measurements.

I met Einthoven for the first time a few days before the opening of the Physiological Congress in Brussels in 1904. I wrote to him from Paris where I was at the time, and then I stopped at Leyden to visit him. I saw at the same time Einthoven and his new instrument, the string galvanometer, which later became known the world over. Einthoven had just completed the construction and installation of his instrument. He was enthusiastic over his extraordinary success, with visions of the possibilities that were open. What I saw there seemed to me unattainable.

After inspecting the laboratory we went together for a walk in the suburbs of Leyden. With great pleasure I recall our long discussions of the importance and the future of electrophysiology. I was glad to find in him support of my idea that electrophysiology must not only go further in studying the nature of animal electricity, but that, first of all, it must enter as a new method of investigation into all branches of physiology. Every organ of the body, so far as it represents a collection of excitable elements, must be studied by the electrophysiological method, because every excitable tissue functions as a source of electricity at the moment of the excitation.

Beginning with the first meeting with Einthoven our correspondence started and continued till the end of his life. I shall speak only briefly of his scientific merits, for they are still too fresh in everybody's mind.

First of all he is the creator of electrocardiography. All methods proposed by him, his standardization, his electrodes, his three leads, his triangle, his terminology, all these are based on theory and at the same time are highly practical; they will all remain in electrophysiology, if not forever, at least for a long time.

Later Einthoven demonstrated how to experiment with the currents

of nerve fibers. He was the first to demonstrate the action current produced by heart contractions in the depressor nerve in its centripetal nerve fibers. He was the first to demonstrate the action current in the sympathetic nerves.

Later he did not adopt the method of amplification with vacuum tubes. He told me several times that by perfecting his string galvanometer he would obtain more correct curves than with vacuum tubes. During the last years of his life he was working with strings 1/100 of a micron thick. Such strings are so thin that they show Brownian movement due to the bombardment of air molecules. The weight of such strings is so small that they could show all the vibrations produced by a voice. They vibrate together with the surrounding air. Photographic records of such strings in air were the best and simplest method of recording sound waves. Einthoven obtained beautiful curves of vowels, for example. The strings were so thin that the question rose as to how they could be seen and projected; Einthoven wrote a special paper on this question.

Einthoven did not write much. All his works are distinguished by thoroughness, completeness and particular beauty of execution.

It happened that I used to meet Einthoven comparatively often. Due to certain circumstances I used to stay with his family, in his house, for several weeks, and could observe his life. His was a pleasant life. He experienced real happiness achievable only by great investigators who tread new scientific paths. He was happy in his family life, surrounded by the love and kindness of his family and friends. He was given the greatest scientific honors and signs of distinction, including the Nobel Prize. But he remained the same simple, frank, direct man. His definiteness and frankness, seen in his work, could be discerned also in the features of his character. His frankness compelled him to fight all he considered unjust, and on the other hand this same frankness made him welcome all who were worthy of his support.

One of the features of his character, which I myself also possess, closely united us, that is, the love to joke. He liked jokes, liked to laugh, liked also to make friendly fun of people and did not object to being made fun of himself. Often I could observe that a joke would lead him to a remark revealing his noble side. A few years ago I was glancing through Pflüger's *Archives* and noticed that the paper in which, for the first time electrocardiograms of a string galvanometer were printed, would soon be 25 years old. I sent Einthoven on this occasion a joking letter. I wrote him: "Dear Einthoven: I am writing this letter not to you, but to your dear and honorable string galvanometer, and therefore I address him. Dear, honorable galvanometer, I just learned that you have a jubilee, that 25 years ago you traced the first electrocardiogram. I congratulate you. I do not

want to keep away from you the fact that I am fond of you in spite of your being sometimes very tricky. I marvel at how much you have accomplished during 25 years. If we should count the number of meters and kilometers of photographic paper used for records with your strings in all parts of the world, the resulting figures would be enormous. You created a new industry, you have philological merits too; we owe you the birth of new words like electrocardiogram."

At the end of this long letter which I do not want to reproduce in full, I said: "And so, my dear and honorable galvanometer, I embrace you and beg you to transmit to Einthoven my congratulations." Then I added: "Dear Einthoven, I beg you to read this letter to the string galvanometer, since it can write but it can't read."

In a short time I received an answer from Einthoven; he wrote: "I have carried out precisely your request and read to the galvanometer your letter. Apparently he listened and took in with pleasure and joy, all that you wrote. He hadn't suspected that he had done so much for humanity, but at the place where you said he does not know how to read, he all of a sudden became furious, so that I and my family became even alarmed. He cried: 'What, I can't read? It's a terrible lie. Do I not read all the secrets of the heart?' I calmed him and advised him in the future to continue to do only one thing—to work and to toil as much as he could for the benefit of humanity, and not to think of gratitude."

This idea of work for humanity I saw in Einthoven very often in different ways. When in Stockholm in 1924 he received the Nobel Prize he ended his speech with the following words: "Es ist ein neues Kapitel der Lehre der Herzkrankheiten hinzugefugt worden nicht durch die Arbeit eines einzigen, sondern durch diejenigen vieler talentvoller Männer, die bei ihren Forschungen sich durch keine politischen Grenzen haben beeinflussen lassen und, über unsere Erdoberfläche verbreitet, Ihre Krafte einem idealen Zwecke haben widmen wollen der Entwickelung der Wissenschaft, wodurch schliesslich der leidenden Menschheit genützt worden ist."*

A few months before his death in 1927, when nobody was suspecting anything out of the way I met him in Leyden. He was gay and brisk as usual. He gave me as a souvenir an excellent photograph of himself. At the station when we were parting, suddenly he became serious: "Perhaps we may never meet again." He proved to be right.

In memory of today's talk may I ask to be allowed to send after I reach home a copy of this picture of Einthoven to the cardiac department of the Massachusetts General Hospital?

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*A new chapter in the scientific knowledge of heart disease has been introduced, not through the work of a single person, but *through the labor of many* talented men who have carried out their investigations unlimited by any political boundaries. These individuals over the whole world have dedicated their energy to an ideal consisting of the development of knowledge which ultimately benefits suffering mankind.

THE EFFECT OF THE INTRAVENOUS ADMINISTRATION OF DIGITALIS IN PAROXYSMAL TACHYCARDIA OF SUPRAVENTRICULAR ORIGIN*†

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ANN ARBOR, MICH.

IN THE great majority of instances simple paroxysmal tachycardia occurs in attacks, which, if they do not terminate spontaneously within a few hours, can be brought abruptly to an end by pressure upon the carotid sheath or by some other simple procedure involving vagus stimulation. Consequently, there is ordinarily little need for the administration of drugs in this disorder, and comparatively few careful studies of the effects of medicinal therapy have been made.

There is considerable evidence that both digitalis and quinine, or quinidine, are not infrequently effective in restoring the normal cardiac mechanism. When the administration of these or other drugs by mouth is followed after a brief interval by the return of sinus rhythm, it is, however, difficult, unless this effect is obtained repeatedly, to exclude the possibility that the attack may have ended spontaneously rather than as a result of the treatment. When on the other hand, the paroxysm ends abruptly immediately after the intravenous injection of a drug, there can be little doubt as to its effectiveness.

Singer and Winterberg[2] have reported a number of instances in which the intravenous administration of quinine (0.4 to 0.75 gm.) was followed at once or within a few minutes by cessation of the abnormal cardiac mechanism. There was usually a striking fall in heart rate preceding the termination of the paroxysm. Iliescu and Sebastiani[3] also have reported an instance in which quinidine by mouth strikingly reduced the rate of the ectopic rhythm. It has also been observed that strophanthine by vein or digitalis by mouth will occasionally abolish the abnormal rhythm; there is, however, so far as we know, no clear evidence that digitalis preparations given intravenously may produce pronounced slowing of the heart rate followed by cessation of the paroxysm, just as in the case of quinine. We wish therefore to report two cases in which these effects were observed.

OBSERVATIONS

An American housewife (E. T.), aged 54 years, was admitted to the hospital on March 3, 1925, complaining of attacks of rapid heart action which began after an attack of rheumatic fever at the age of eighteen years. The attacks occurred every two to four months and varied in duration from fifteen minutes to thirty hours. They were accompanied by palpitation and giddiness and were followed by

*From the Department of Internal Medicine, University of Michigan Medical School.

†The observations reported here were referred to briefly in an article read at a meeting of the Association of American Physicians, May 1926. (1).

severe nausea and vomiting. Cardiovascular examination showed moderate enlargement of the heart and low-grade aortic insufficiency. The peripheral vessels were moderately sclerosed, the blood pressure was 145 mm. Hg. systolic, 65 mm. Hg. diastolic, and the electrocardiogram showed pronounced left ventricular preponderance. The thyroid gland was moderately enlarged and there were rather questionable signs of mild thyroid intoxication. The cardiac function was good.

The cardiac mechanism was normal until March 11, when the heart rate suddenly rose to 200 or more per minute and the symptoms described by the patient as characteristic of previous attacks developed. A summary of the observations made at this time is given in Table I. The rates given in the table were computed from

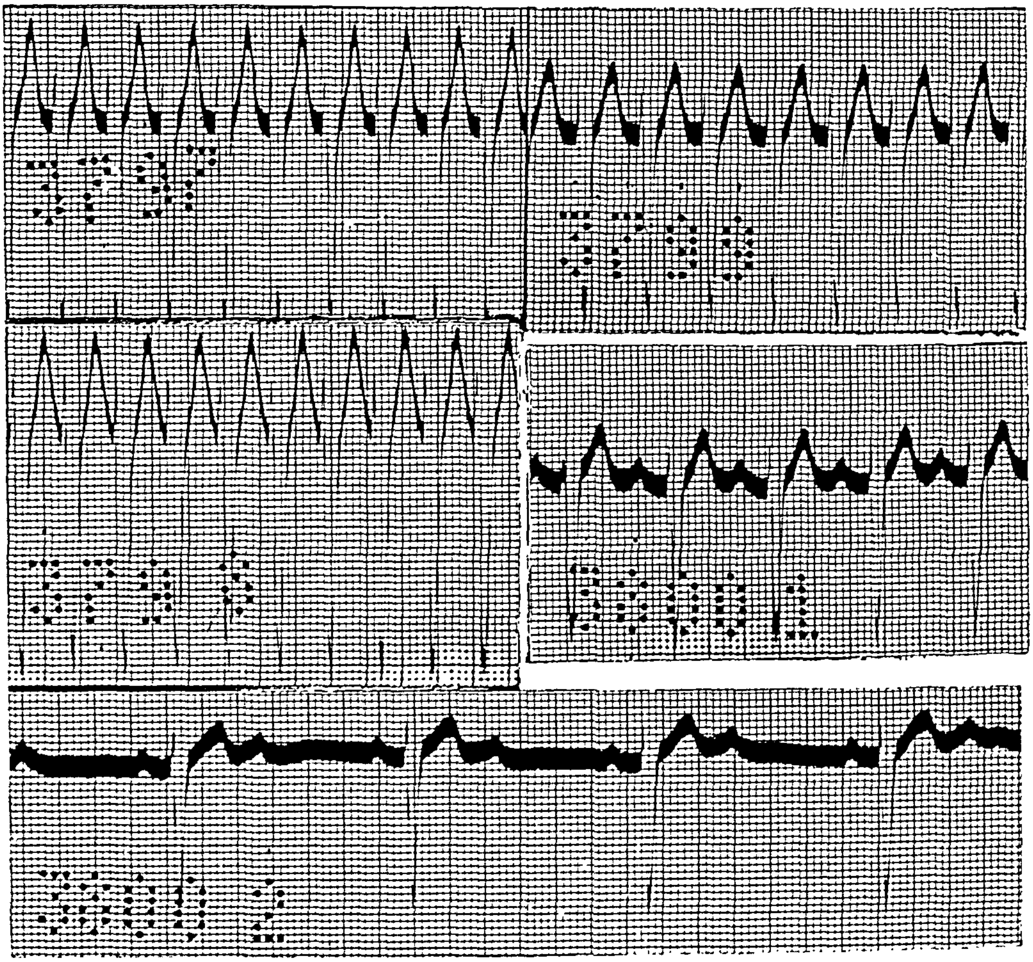

Fig. 1.—First patient; E. T. All curves taken by a chest lead, manubrium to ensiform. Ords. 1 cm. equals 1 millivolt. Abs. 1 div. equals 0.04 sec. 3797; control; rate 205 per minute. 3798; after 0.2 gm. quinidine; rate 210; QRS interval slightly increased. 3799; after digifolin 10 c.c. intravenously; rate 174. 3800-1; after second dose of digitalis; normal rhythm. 3800-2; 2-to-1 heart-block during an attack of nausea; taken immediately after 3800-1.

electrocardiograms which were taken at brief intervals throughout the duration of the attack. In order to avoid the muscle tremor which distorted the curves taken in the usual manner a chest lead (manubrium to ensiform) was employed. The form of the ventricular complex indicated that the abnormal rhythm was of supraventricular origin, but no auricular deflections were visible. Bilateral pressure upon the carotid sheaths and ocular pressure were without effect. The intravenous administration of quinidine (0.2 gm.) had no effect upon the heart rate, but produced minor changes in the form of the ventricular complex and increased the

QRS interval some 0.03 or 0.04 second (Fig. 1). A proprietary preparation of digitalis (10 c.c. of this preparation are approximately equivalent to 1 mg. of ouabain) was then given intravenously. An immediate and striking fall in heart rate resulted. A half-hour later a second dose (5 c.c.) was given; at this time the movements of the galvanometer string were under observation. There was a further slowing of the rate followed immediately by cessation of the abnormal rhythm. Nausea and vomiting followed and during the attacks of vomiting two-to-one heart-block was present (Fig. 1). The nausea continued for 48 hours, diminishing gradually. The patient had no further attacks of tachycardia while she remained in the hospital.

The second patient, E. M., a factory worker, aged 32 years, was admitted to the hospital Jan. 5, 1926. He was suffering from an attack of rapid heart action, associated with palpitation, dyspnea, and exhaustion, which began 12 days before. He had his first attack while playing baseball at the age of 14 years. At first the attacks came only twice a year and lasted only a few hours; but for three years he had had from six to nine attacks annually, each lasting from eight to twelve days. The attacks usually came on during exertion, but occasionally they began while he was walking or sitting down, or awakened him from sleep. They were accompanied by severe prostration and dyspnea and he was forced to go to bed; in the longer attacks he suffered from insomnia and profuse sweating at night, and, after four or five days, from cough with thick tenacious sputum. There was a clear history of rheumatic fever five years before admission.

TABLE I

E. T.—PAROXYSMAL AURICULAR TACHYCARDIA

E.C.G. NO.	DATE	TIME	MEDICATION	TIME SINCE LAST DOSE	HEART RATE	REMARKS
3794	3/11/25	12:30 P.M.			211	No digitalis since 3/3/25
3795	3/11/25	12:31 P.M.			208	During bilateral vagus pressure
3796	3/11/25	12:32 P.M.			206	During ocular pressure
3797	3/11/25	12:45 P.M.			205	Control
3797	3/11/25	12:46 P.M.	Quinidine grs. iii I. V.		208	Taken during injection of quinidine
					208	Taken after injection of quinidine
3798	3/11/25				206	Last curve eight minutes after
				8 min.	210	
	3/11/25	1:18 P.M.	Digifolin 10 c.c. I. V.			
		1:25 P.M.		7 min.	176	
3799	3/11/25	1:26 P.M.		8 min.	173	
		1:27 P.M.		9 min.	174	
3800	3/11/25	1:47 P.M.	Digifolin 5 c.c. I. V.		107	Further slowing followed immediately by normal rhythm. Nausea and vomiting with partial heart-block during attacks of vomiting.

The heart rate was approximately 208 per minute; the precordium and the engorged neck veins throbbed violently. The patient was obviously short of breath and there was slight edema of the sacrum, a slight hydrothorax on the left side, râles at the lung bases, engorgement of the liver, and a small collection of ascitic

fluid. The heart was considerably enlarged to the left (left border 3 cm. outside the nipple line and 16 cm. to the left of the midline); embryocardia was present, but there were no murmurs. The urine contained a small amount of albumin and there was a slight leucocytosis. The electrocardiogram showed small ventricular complexes with broad initial deflections; no auricular deflections were visible.

TABLE II

E. M.—PAROXYSMAL AURICULAR TACHYCARDIA

E.C.G. NO.	DATE	TIME	MEDICATION	TIME SINCE LAST DOSE	HEART RATE	REMARKS
5400	1/6/26	11:15 A.M.			211	Pressure on both vagi without effect
5401	1/6/26	11:30 A.M.			210	Control
	1/6/26	11:31 A.M.	Philocarpine 1/8 gr. I. V.			
5401	1/6/26				200 to 210	Taken shortly after injection of pilocarpine
5402	1/6/26	11:45 A.M.			200 to 204	During ocular and vagal pressure
5403	1/6/26	12:06			204	Control
	1/6/26	12:07	Apomorphine Grs. 1/10 by hypo.			
5403	1/6/26	12:28			204	
5411	1/7/26	1:05 P.M.			210	Control
	1/7/26	1:07 P.M.	Digifolin 10 c.c. I. V.			
5412	1/7/26	1:17 P.M.		10 min.	190	
5413	1/7/26	1:30 P.M.		23 min.	187	
5414	1/7/26	2:00 P.M.		54 min.	189	
	1/7/26	2:15 P.M.	Digifolin 5 c.c. I. V.			
5415	1/7/26	2:25 P.M.		10 min.	182	
5416	1/7/26	2:50 P.M.		35 min.	185	Change in form of ventricular complexes
	1/7/26	3:40 P.M.		85 min.	-	Normal rhythm reported
5421	1/7/26	4:25 P.M.		130 min.	88	Normal rhythm

A summary of effects of various procedures upon the abnormal rhythm is given in Table II. While each of these procedures was carried out the galvanometer string was watched, and records were made at frequent intervals. The rates given are computed from these records. Ocular and vagal pressure were without effect. Pilocarpine intravenously and apomorphine hypodermatically, which induced vomiting, also failed to abolish the abnormal rhythm or to modify the heart rate. As in our first patient intravenous administration of a proprietary preparation of digitalis was followed immediately by a striking drop in the heart rate (Fig. 2) and a further fall in rate followed a second smaller dose. Thirty-five minutes after the second dose the ventricular complexes changed in form, and assumed the shape of the complexes recorded after the normal rhythm returned (Fig. 3). It seems clear that the broad initial deflections of the complexes recorded earlier was the result of defective intraventricular conduction dependent upon the rapid rate, and that when the rate fell the conducting system recovered its normal conductivity. Recovery did not take place at once for the rate was actually slightly higher when the change in the form of the complexes was observed than it was twenty-five minutes earlier. It seems possible, therfore, that there was some tendency to cumulative fatigue of the intraventricular conducting system and that the immediate previous history of these tissues and not merely the length of the preceding diastole was a

factor in determining intraventricular conductivity. Although the return of the normal rhythm was somewhat delayed, there can be little doubt that it was the result of the treatment. We have observed that when digitalis or ouabain is given intravenously in auricular fibrillation there is an immediate drop in the ventricular rate, but the maximum effect does not appear as a rule until two or three hours after the drug is given. Following the return of normal rhythm the heart gradually decreased in size and there was a pronounced diuresis with a loss of 31 lbs. in weight. Beginning on January 9 the patient received 4 c.c. of the standard tincture of digitalis daily for a period of eight days without developing toxic symptoms. He had no further attacks of tachycardia while under observation; an electrocardiogram taken on Jan. 15 showed occasional ventricular extrasystoles with retrograde stimulation of the auricles; the ventricular complexes were not remarkable except that the T-deflections were inverted probably as a result of the administration of digitalis.

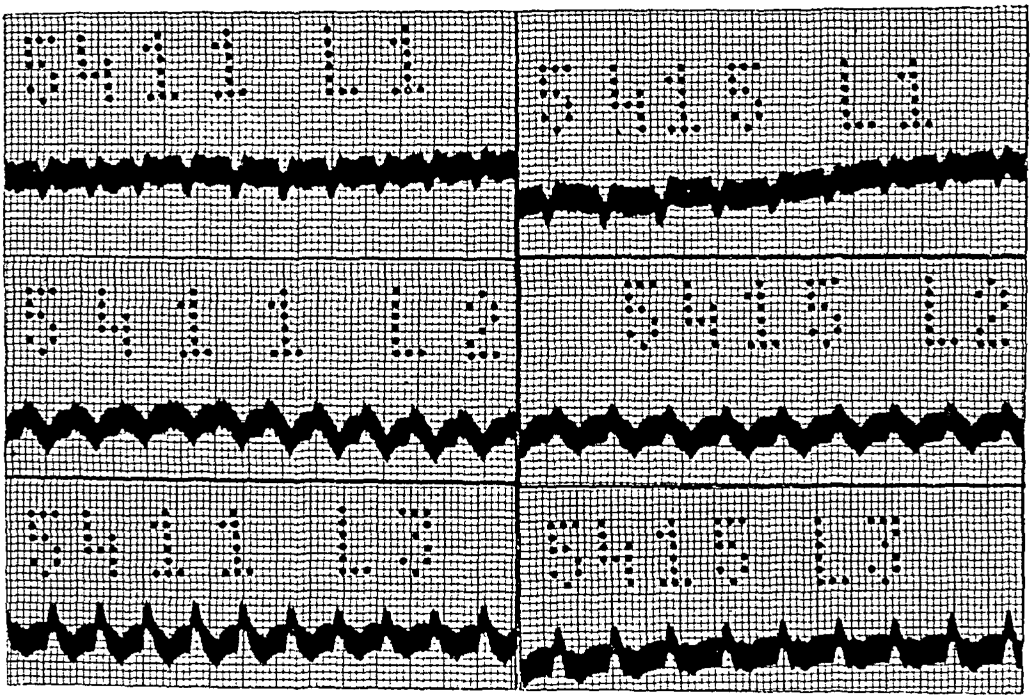

Fig. 2.—Second patient; E. M. The three standard leads. 5411; control; rate 210 per minute. The ventricular complexes are small; the initial deflections, broad. 5415; 10 minutes after digifolin 10 c.c. intravenously; rate 182.

DISCUSSION

The mechanism by which digitalis slowed the rate of the ectopic rhythm and finally abolished this rhythm in our two patients is obscure and must remain so until the nature of paroxysmal tachycardia is better understood. The effects of digitalis upon the heart are complex and they have not been completely investigated. The increase in vagal tone which it induces tends to diminish the rate of stimulus production within the sinus node and within the atrio-ventricular node, and to depress the conductivity of the junctional tissues. It reduces the refractory period of the auricular muscle, and thus improves intra-auricular conduction when the rate of beating is so rapid that the excitatory process is advancing through partially refractory tissue.[4]

By its direct action upon the cardiac tissues, as opposed to its indirect effects exerted through the vagus, digitalis lengthens the refractory period of the auricular muscle,[4] depresses the conductivity of the junctional tissues, and enhances the rate of stimulus formation in those centers which lie below the auriculo-nodal junction.

The first question that arises in the study of any digitalis effect is whether this effect is due to a direct action of the drug upon the heart muscle or to an increase in vagal tone. This question can be answered by the administration of adequate doses of atropine, but in the present instance this procedure was not carried out because the condition of

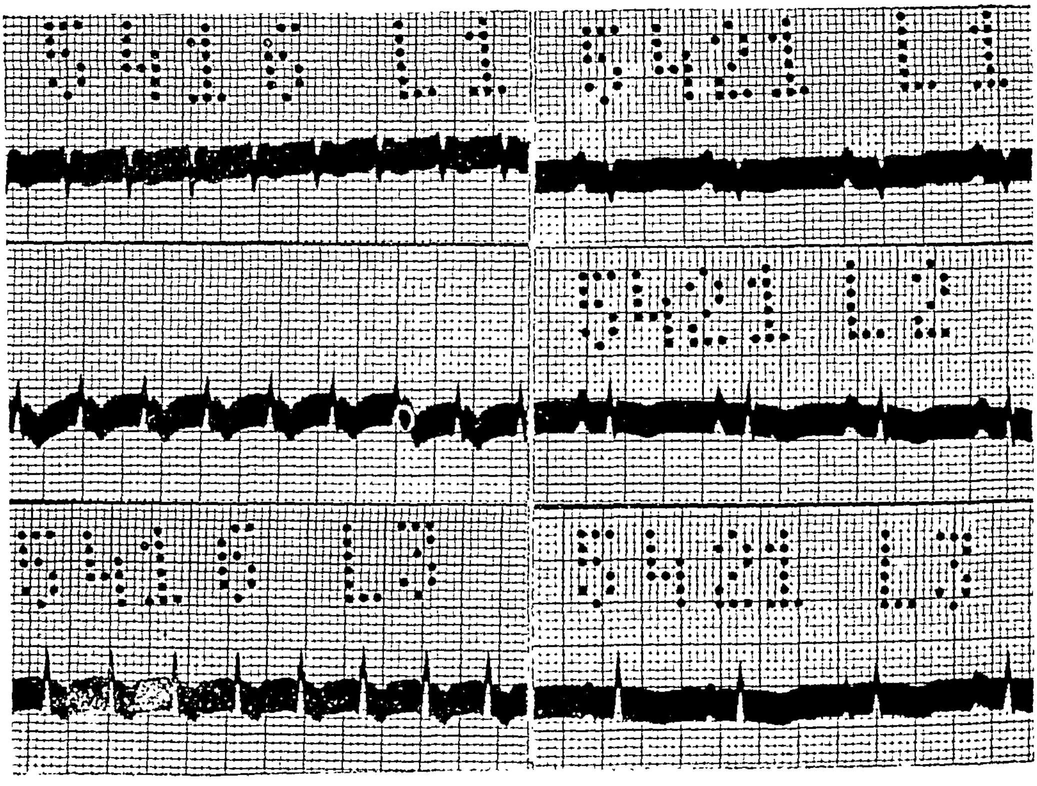

Fig. 3.—Second patient; E. M. The three standard leads. 5416; the ventricular complexes have now assumed the form which they showed after normal rhythm returned; rate 185. 5421; normal rhythm rate 88.

our patients made any medication which might tend to prolong the abnormal rhythm inadvisable. The fact that pressure upon the carotid sheath and upon the eyeballs was without effect upon the ectopic rhythm in both patients, and that pilocarpine, which stimulates the vagal endings, and apomorphine which stimulates the medullary centers, were without effect in one of them does not necessarily mean that the digitalis effects under discussion were non-vagal in origin. The failure of these procedures in some cases of paroxysmal tachycardia and their success in others is probably due in greater measure to differences in the grade of vagal stimulation which they induce than to variations in the susceptibility of the abnormal cardiac mechanism to

vagal influence. The effects of these methods of stimulating the vagus are equally variable when sinus rhythm prevails.

Opposed, however, to the view that digitalis slowed the rate of the paroxysmal rhythm in our patients by its vagal rather than by its direct effects upon the cardiac muscle is the fact that pressure upon the carotid sheath and other methods of stimulating the vagus do not ordinarily slow the rate of the ectopic rhythm in paroxysmal tachycardia even when they abolish the abnormal mechanism. Occasionally, however, there is very slight slowing involving only two or three cycles, just at the end of the paroxysm.[7] Exercise which reduces vagal tone is also usually without effect although Wenckebach and Winterberg[8] mention cases in which an increase in rate was observed following exertion.

In view of these considerations it is impossible to decide whether the effects produced by digitalis in paroxysmal tachycardia are vagal or

Fig. 1.—Curves from a case paroxysmal tachycardia of auricular origin. 1619; chest lead, manubrium to ensiform. An attack of paroxysmal tachycardia brought to an end by pressure upon both eyeballs. The attack ends with a blocked auricular beat. At the end of the record a new attack begins. 1620; Same patient, lead II. An attack of paroxysmal tachycardia ends spontaneously with a blocked auricular beat. At the end of the record a new attack begins.

non-vagal in origin until it is known whether or not they are altered by the administration of atropine.

The failure of quinidine to abolish the abnormal rhythm or to slow its rate in one of our patients raises the question as to whether the cardiac mechanism in cases in which digitalis is effective differs from that present in cases in which quinidine or quinine is effective. It is possible that the dose given was too small to produce the characteristic effects of the drug. Previous experience with the intravenous administration of quinidine made us hesitate to give a larger amount because of the marked depression of intraventricular conductivity which results when the ventricular rate is greatly accelerated. The dose given is sufficient to reduce conspicuously the rate of the circus rhythm in auricular flutter and in auricular fibrillation although the fall in rate

is more or less proportional to the original rate. Thus, in four cases of auricular flutter with original rates of 360, 291, 270, and 210 the reduction in rate produced by 0.2 gm. of quinidine given intravenously amounted to 75, 55, 52, and 23 beats per minute, respectively. In auricular fibrillation the fall in circus rate is usually 100 cycles per minute or more.

The observations recorded in this article were prompted by the study of another patient with paroxysmal tachycardia of supraventricular origin, but without visible auricular waves in the electrocardiogram. In this instance 0.5 gm. of quinine intravenously reduced the heart rate from 250 to 204 per minute within a period of two minutes; the abnormal rhythm was not, however, abolished. A digitalis preparation (digifolin 5 c.c.) was then given intravenously. The attack came to an end about one hour later, but unfortunately no electrocardiograms were made between the time when the digitalis was given and the end of the attack. These observations lead us to suspect that the failure of quinidine and the effectiveness of digitalis in the first case described in this article was probably not due to any peculiarity of the underlying mechanism, and suggest that the two drugs may possibly be given together with advantage in stubborn cases of paroxysmal tachycardia.

Because of the similarity of the effect of quinidine and quinine upon the heart rate in paroxysmal tachycardia to their effect upon the rate of the circus rhythm of auricular flutter and auricular fibrillation, it has been suggested that paroxysmal tachycardia is also due to circus contraction.[3] The effect of digitalis upon the rate of the ectopic rhythm in paroxysmal tachycardia is, on the other hand, just the reverse of its effect upon the circus rate in auricular flutter and auricular fibrillation, for although the change in the rate of the circus rhythm which it produces in these conditions is as a rule not profound, nevertheless there is a definite tendency for the rate to go up, and flutter can usually be converted into fibrillation by full digitalization. It is true that in rare instances of fibrillation, possibly because the direct effect of digitalis upon the auricular muscle overbalances its vagal effect, slight slowing of the circus rate results,[4] but this effect has not been observed in flutter, in which the gap of responsive tissue is wider than in fibrillation, and it does not seem to offer a reasonable explanation of the effect of the drug in paroxysmal tachycardia.

It has also been suggested that quinidine and its allies slow the heart rate in paroxysmal tachycardia and abolish the ectopic rhythm by lengthening the refractory period and thus rendering very early responses impossible.[7] It is conceivable also that the depression of excitability produced by these drugs might in some manner account for the effects in question. Digitalis, however, although its vagal and its direct effect upon the refractory period are in opposite directions, tends on

the whole to shorten the refractory period of the auricle in man; upon excitability it has no known effect.

In so far therefore as the effects of digitalis and quinidine upon the *auricular muscle* are known, there are apparently no similarities between them which can explain why they should act alike in paroxysmal tachycardia of auricular origin. It must be admitted, however, that the observations here reported do not demonstrate that these two drugs do have the same effect in this condition, for the effect of quinidine was not tested in one of the patients studied, and it was not adequately tested in the other, and the observations upon the third patient mentioned although suggestive were inconclusive. It was, furthermore, impossible to determine in these patients whether the abnormal mechanism was of auricular or of atrio-ventricular origin. Finally, it must be pointed out that if, as we suspect, the two drugs are found when adequately tested to have the same effect in one and the same case, it must still be admitted that this effect may be produced by digitalis in one way and by quinidine in an entirely different way, or that the effect in question may be produced by a similar, but as yet unknown effect of both drugs upon the cardiac tissues.

Both quinidine and digitalis depress the conductivity of the atrio-ventricular tissues, although the effect of the former is somewhat diminished and under certain conditions entirely obscured by the reduction of vagal tone which it induces. The question arises therefore as to whether a similarity in the effects of these drugs upon the junctional tissues has any bearing upon their effect in paroxysmal tachycardia. It is quite possible that digitalis was effective in both of our patients, and it is conceivable that quinidine was ineffective in the one instance in which it was given, because the abnormal rhythm was of atrio-ventricular origin. In this connection we may call attention, however, to a feature of paroxysmal tachycardia which has been insufficiently emphasized; we refer to the great difficulty of inducing block while the abnormal rhythm is present. When one considers the pronounced tendency to heart-block that is present in auricular flutter, even when the auricular rate is only slightly above that ordinarily seen in paroxysmal tachycardia, the rarity with which heart-block is induced in the latter condition by pressure upon the carotid sheath, or upon the eyeball, or by the administration of digitalis is astonishing. It is still more so when one considers that the P-R interval in paroxysmal tachycardia is frequently considerably increased.

As an example of the difficulty of producing block in paroxysmal tachycardia we may cite the observations made upon our first patient. After the second dose of digitalis the paroxysm ended and nausea with temporary high grade partial heart-block occurred. It seems strange that heart-block did not occur while the rapid rhythm was present, although it is impossible to rule out the possibility that in this instance

the site of origin of the abnormal rhythm was in the junctional tissues below the region where digitalis and vagal block occur. It should be pointed out that vagal and digitalis block does occur in rare instances of paroxysmal tachycardia; such cases have been described by Wenckebach and Winterberg[6] and we have ourselves seen such a case. Nevertheless it is extremely rare. The explanation is obvious although its significance is not clear. The susceptibility of the ectopic rhythm to vagal stimulation is ordinarily so great that a degree of vagal stimulation insufficient to produce block brings the abnormal cardiac mechanism to an end. Not infrequently, however, when auricular paroxysmal tachycardia is abolished by vagal stimulation, the last auricular beat of the ectopic rhythm is blocked (Fig. 4); that is, the onset of block and the end of the paroxysm occur at the same instant. We cannot therefore dismiss the possibility that in some instances of paroxysmal tachycardia vagal stimulation brings the abnormal rhythm to an end by depressing the conductivity of the junctional tissues, nor can we deny the possibility that digitalis and quinidine may slow the abnormal rhythm and finally abolish it in the same way.

In view of the character of the evidence bearing upon this problem which is at present available, and in view of the great difficulty of harmonizing many observations with the possibility suggested above it does not seem profitable to pursue the subject further at this time. We bring the matter up in order that observations bearing upon it may be made as the opportunities arise. It is desirable first of all to know whether the effect of digitalis described is influenced by the administration of atropine; whether it occurs in paroxysmal tachycardia of atrioventricular origin only, or whether it occurs in all types of paroxysmal tachycardia of supraventricular origin; whether it is a rare or a common phenomenon; and whether quinidine and digitalis may both slow the rate of the ectopic rhythm in one and the same case.

SUMMARY

In two cases of paroxysmal tachycardia of supraventricular origin the intravenous administration of digitalis produced a pronounced slowing of the heart rate followed by the return of the normal sinus rhythm.

The significance of these observations is discussed.

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THE BLOOD VESSELS AS A POSSIBLE SOURCE OF VISCERAL PAIN

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INTRODUCTION

Even before the advent of local anesthesia it had been noted that the abdominal viscera were insensitive to many forms of stimulation which caused severe pain when applied to somatic tissues. As operations under local anesthesia became more frequent it was shown that cutting, crushing and burning of the viscera failed to elicit pain reactions from the conscious patient. Again, the pain was not uncommonly experienced in areas at some distance from the diseased viscus and was frequently accompanied by vascular changes, hyperesthesia of the skin and muscles and muscular spasm in the body wall. In the face of these observations was the obvious fact that visceral disease was often characterized by severe pain.

Two schools of thought arose to explain the apparent discrepancy between these observations. The first, whose foremost exponent has been Sir James Mackenzie[1] proceeded on the theory that there were no true pain pathways from the viscera to the higher centers. It was pointed out that the "referred" phenomena, expressing themselves in the somatic tissues of the body wall, always bore a definite relation to the diseased viscus, in that the same segment of the spinal cord supplied both the somatic area involved and the organ at fault. It was assumed that even in the absence of true pain pathways, impulses from the viscera might "overflow" into the common pain pathways from somatic tissues and thus give rise to sensations of pain that would be ascribed by the subject to the peripheral distribution of the particular pathways so involved. Disease of an internal organ, then, was silent or painful, depending upon whether or not afferent impulses from the organ overflowed into somatic pathways of specialized pain conduction. This theory seemed to be consistent with many clinical observations and explained in a beautiful manner the phenomena of referred pain, hyperesthesia and muscle spasm.

Although this theory was of considerable importance in calling attention to the value of pain analysis in diagnosis and did much to stimulate interest in visceral pain, certain objections to its full acceptance became evident. The accuracy with which a patient localized his pain as deep-seated in certain cases of gall-stone colic, distention of the bladder or renal pelvis, or the pain caused by a large bolus of food in the esophagus and many other clinical observations seemed to argue against the assumption that pain of visceral origin is of necessity expressed in somatic areas. Thus a second school of thought

arose, by which it is claimed that true visceral pain exists, and can be elicited by a proper ("adequate") stimulus.

The work of Hurst,[2] Ryle,[3] Payne and Poulton[4] and many other investigators has laid emphasis on abnormal degrees of tension in the walls of hollow viscera as constituting "adequate" stimuli for true visceral pain. It has been shown that under proper conditions, spasm of smooth muscle and increased intramural tension from abnormal distention, are each capable of giving rise to afferent impulses which are experienced as pain and ascribed by the subject with a fair degree of accuracy to the internal organs rather than to the somatic tissues of the body wall.

THE CONTROL OF BLOOD VESSEL CALIBER

The function of any organ must be dependent to a high degree on the caliber of its blood vessels. Although the smooth muscle of blood vessels has a tonus of its own and may be influenced by various metabolic substances in the circulation, such as adrenalin, the smooth and harmonious functioning of the vessels in various parts of the body must be dependent upon nervous control. The effector units of this control are a part of the "autonomic" nervous system and have been termed "vaso-motor" neurons. These neurons affect the degree of smooth muscle contraction, but must not be considered "motor" in the same sense that we apply this term to motor neurons supplying voluntary muscle. In case the motor neuron to skeletal muscle is divided, an immediate, flaccid paralysis results, followed later by atrophy of the muscle elements. Division of "vaso-motor" neurons, on the other hand, may be followed by temporary or lasting changes in the vessel caliber, but never results in a true paralysis nor is it followed by atrophy of the smooth muscle. Rather than considering these neurons as being "motor" we might look upon them as association units, subserving a harmonizing and coördinating function.

The blood vessels are thus seen to possess an autonomy of function very similar to that displayed by the gastro-intestinal tract after it has been deprived of its extrinsic nerves. This autonomy and the coördinating function of the extrinsic nerves to blood vessels is well illustrated by Cannon's[5] sympathectomized cats. These animals, from which Cannon had removed the entire peripheral portion of the sympathetic nervous system, maintained an apparently normal circulation under favorable environment, but were extremely sensitive to cold. Cannon attributed their sensitiveness to cold, in part at least, to the animals' inability to reduce the peripheral circulation in the normal manner.

The coördinating functon of the extrinsic nerves of the blood vessels must be dependent, not only on the autonomic neurons, but on an equally important system of afferent neurons from all parts of the body as well as from the walls of the vessels themselves. The afferent

side of the "Visceral Nervous System" has been but little studied. That it exists and that it serves an important function in various reflexes and body adjustments is indicated by the work of Carlson and Luckhardt,[6] and many other investigators. We now believe that there are visceral afferents from visceral tissues in all parts of the body, including the blood vessels. The actual demonstration of afferent fibers from vessels has lagged behind physiological evidence, but sufficient evidence of their existence has been afforded by study of degeneration changes following division of perivascular plexuses, and the demonstration of various types of receptor end-organs, including typical Pacini corpuscles, in the walls of blood vessels.

The similarity in nervous control of the smooth muscle of blood vessels and the smooth muscle of other visceral organs, together with the clinical observation of both distention and spasm of vessel walls, suggests that true visceral pain may arise from blood vessels. This reasoning by analogy is supported by experimental and clinical evidence presented in this paper.

EXPERIMENTAL EVIDENCE OF PAIN FROM BLOOD VESSELS

Spiegel and Wassermann[7] observed that slight distention of the ascending aorta elicited pain reactions in experimental animals. Odermatt[8] demonstrated that pain reactions may be elicited by distention of arteries of any caliber. Bazett and McGlone[9] showed that simple puncture of the wall of an artery was painful. They asserted that the pain was characteristically of a dull, aching and unbearable quality, frequently accompanied by uncontrollable reflex reactions, such as sweating, sudden sensations of warmth or cold, faintness or even loss of consciousness. Various investigators have shown that when a spasm of an artery is produced by injection of barium chloride a very intense pain invariably results. Odermatt[8] was able to elicit pain reactions by various manipulations of blood vessels and attributed the pain to change in tension acting on the perivascular endings of visceral afferent neurons. He concluded that pain reactions following injection of irritating substances arose in the capillaries. He was inclined to regard the spasm of blood vessels and the resultant pain as comparable with intestinal colic.

OBSERVATIONS OF SIMILAR PHENOMENA IN SURGICAL PROCEDURES

In the injection treatment of varicose veins I have noted two types of pain that appear to arise in the vein walls rather than from somatic tissues. The first is a slight aching sensation elicited most commonly when a small group of varices is isolated by pressure from connecting veins and the fluid put in under pressure so as to distend the vein. The pain begins during the injection and is relieved promptly by withdrawing some of the fluid into the syringe so as to lessen the tension in the vein. The second type of pain is elicited when certain irritating

solutions, such as a salt-sugar mixture, are used and the injection made with the patient standing. This pain is described as a deep, aching pain. It comes on after the injection is complete, radiates down the leg along visible venous channels, and not uncommonly these channels may be observed to diminish in size coincident with the onset of pain having a definite wave-like character. The time factor in the appearance and duration of this pain is of a remarkable constancy. The pain begins gradually about 70 seconds after the injection is begun, increases in severity for about forty-five seconds, maintains its height for a little over a minute and then fades, so that at the end of four minutes from the time of injection the pain has practically disappeared. The absence of evidence of leakage around the needle together with the wave-like character of the pain seems to indicate that the pain is due to a spasm of the smooth-muscle elements in the vein walls.

During operations under novocain anesthesia the patient may complain of pain when an artery is clamped. Ligation of the main gastric arteries is almost invariably painful. The pain is often intense, usually of short duration and described as diffuse rather than being accurately localized. If an artery showing this sensitiveness is stretched laterally or pulled upon, the patient will frequently complain of pain. On several occasions I have noted pain from clamping arteries in an operative field in which the local anesthesia seemed otherwise entirely satisfactory.

Recently during an operation under spinal anesthesia in which the anesthesia was incomplete, it was noted that the patient seemed to experience but little pain when the skin was incised, but complained bitterly when an artery was clamped and ligated.

CUTANEOUS STIMULATION FOR RELIEF OF VISCERAL PAIN

As far back as medical history extends we find records of the use of various forms of cutaneous stimulation for the relief of deep-seated pain. Rubbing, heat, cold, cuppings, leeches and counter-irritants of all kinds have been utilized in the treatment of visceral pain. Perhaps the commonest form of cutaneous stimulation is the application of heat over the painful area. We know from actual experiment that the penetration of heat is not great, yet the patient frequently experiences a marked and prompt lessening of his pain. Nor is it reasonable to assume that there occur any immediate changes in the underlying inflammatory lesion. It is more likely that any effect on the pain produced by the external application of heat is due to reflex changes. Wernoe[10] not only showed that visceral stimulation may bring about viscero-cutaneous and vaso-motor reflex changes in the periphery but also demonstrated that cutaneous stimulation was capable of eliciting vaso-motor reactions in the vessels of the viscera. In some of his experimental animals cutaneous stimulation resulted in reflex visceral hyperemia and in others a visceral ischemia.

The prompt change in the character of the visceral pain following cutaneous stimulation, together with the observation that immediate vascular reflexes may occur, seems to argue that certain types of visceral pain may originate in the walls of blood vessels. This argument is by no means conclusive, since we know that smooth muscle of other organs may be reflexly affected by the cutaneous stimulation, yet the argument remains worthy of consideration.

ISCHEMIA AS A CAUSE OF PAIN

Many clinical conditions associated with pain are characterized by localized arterial spasm with a resultant ischemia of the surrounding tissues. This ischemia is commonly held to be the cause of the pain. While it is impossible in the present state of our knowledge to rule out ischemia as a contributing factor in certain cases of pain, I have never been able to convince myself that it is the major factor in many of the pain syndromes for which it has been held responsible.

If one applies an Esmarch bandage and then a tourniquet to his arm for ten or fifteen minutes there is no real pain experienced in spite of the presence of a marked ischemia and a developing cyanosis. One feels a sensation of weight and numbness to which is added, within a few minutes, a fine, vibratory, tingling sensation in the fingers, but no real pain is experienced until the tourniquet is released. Then one feels a rather painful sense of suffusion and sees the extremity flush suddenly as the capillaries fill, followed by stabbing pains that resemble sharp, scattered and intermittent electric shocks.

When an extremity is exposed to extreme cold there follows an ischemia associated with an aching pain. If the pain were entirely due to the ischemia one might expect it to disappear when the extremity was warmed. Experience indicates, on the contrary, that a tingling pain appears, coincident with the return of the circulation, that is often characterized by a painful throbbing sensation which is synchronous with the pulse rate.

PAINFUL SYNDROMES

1. *Raynaud's Disease.* Raynaud's disease is a clinical syndrome characterized by vascular changes in the hands or feet, usually brought on by exposure to cold. The involved extremities become cold, painful and increasingly cyanotic, and, in severe cases, nutritional changes may result in a progressive, dry gangrene of the terminal phalanges. The current explanation of the pain in this syndrome is that it is due to chemical changes in the tissues resulting from the ischemia, which act on the somatic sensory nerve endings to produce pain impulses.

We know little of the underlying mechanisms of this syndrome. Sir Thomas Lewis[11] maintains that the essential factor is a local disease of the digital vessels and holds that vaso-motor reflexes have little or nothing to do with the attacks. If this concept is correct, it naturally throws doubt upon the rationality of the various surgical sympathec-

tomies proposed for the relief of Raynaud's syndrome. Yet, in Lewis' own paper he presents a case which seems to me to throw doubt upon his interpretations. This woman (case 1, Observation 33) developed a typical attack following the exposure of a single finger to cold. The middle finger of the right hand was plunged into cracked ice, while the remainder of the fingers were kept at room temperature. Severe pain developed, followed by a rapidly increasing cyanosis of the fingers of *both* hands. Lewis explains this attack as resulting from the pain stimulation of that particular finger and seems to think that the other fingers were in an abnormal state at the time of the experiment, However, I am unable to see why pain should be accepted by Lewis as a more adequate stimulus for reflex precipitation of an attack in preference to any other unperceived impulse from the vessels or the surrounding tissues of the finger. In fact, it would seem to me that if reflexes could produce the attack under any circumstances, Lewis' position would be materially weakened.

I am inclined to interpret the attacks of Raynaud's syndrome as due to reflexes by way of visceral pathways which result in vascular spasm, and believe that the resultant pain originates in the walls of the vessels. Kuntz[12] agrees with this opinion and says in a personal communication, "It is my opinion that in such conditions as Raynaud's disease the pain is due to spastic contraction of the arteries rather than to lack of blood to the tissues."

2. *Angina Pectoris.* Angina pectoris is another pain syndrome in which the underlying factors are but little understood. It is commonly held that the pain is due to ischemia of the contracting cardiac musculature following spasm of the coronary arteries. The areas to which the referred pain is distributed, however, would seem to point toward the base of the aorta or the coronary arteries as the origin of the pain, rather than the myocardium. I am of the opinion that the pain arises in the walls of the vessels themselves. Certain results of surgical sympathectomy would appear to confirm this opinion.

Most of the surgical procedures, such as those advocated by Jonnesco and Leriche are proposed as palliative measures in that they aim to interrupt afferent pathways from the heart. On the other hand, Coffey and Brown[13] report favorable results from simple extirpation of the superior cervical ganglion. Since the available anatomical evidence ascribes a purely motor function to this ganglion, the only possible explanation of pain relief from this procedure would be that it had prevented motor mechanisms responsible for the pain. The known afferent pathways from the heart by way of the middle and inferior cardiac nerves being intact, there should be no reason why the subject should not experience pain if the causative mechanism still existed after the Coffey operation.

Any case, then, of pain relief in angina pectoris resulting from extirpation of the superior cervical ganglion would confirm the belief

that in that particular instance the attacks had been the result of vascular spasm, and, since the pain pathways remain intact, that the pain was the direct or indirect result of the smooth muscle spasm.

3. *Gastric Ulcer.* Odermatt[8] says, "The pain in gastric ulcer is possibly to be explained by a chemical stimulation of the arteries and veins." This suggestion is interesting but in itself does not appear to be consistent with the periodicity and certain other peculiarities of ulcer pain. Kinsella[14] ascribed the pain of peptic ulcer to pressure changes on the inflamed tissues of the ulcer bed. He showed in an ingenious manner that those conditions which give rise to ulcer pain always produce congestion and vascular changes in the ulcer area. If this be true, it would seem likely that at least a part of the pain might arise in the walls of the vessels, particularly in the presence of inflammation and when the ulcer tissue around the vessels is indurated.

4. *Emboli.* Emboli may cause pain. Certain emboli such as fat and tumor cells may not cause pain, but a large embolus, lodging for instance in a mesenteric artery can give rise to most severe pain and a high degree of "shock." Even small emboli to the brain or lungs may be accompanied by severe pain. That the pain is not due to the resultant infarction is evidenced by the fact that infarcts are frequently found at autopsy when there has been no history of pain. Nor is the pain due to inflammatory changes produced by a lodged embolus since the pain is immediate in onset. It appears more probable that the pain is due to a sudden arrest of the embolus at a vessel bifurcation with an immediate distention at the point of impact and a distending backpressure in the vessel proximal to the obstruction. It is also possible that a reflex spasm of the vessel results, in much the same fashion that spasmodic expulsive efforts follow obstruction of the lumen of the intestine.

5. *Headaches.* Headaches of various types may be due to overdistention or spasm of blood vessels. After the use of amyl nitrate or nitroglycerin to lower blood pressure, or, as I have noted after the intravenous injection of corpus luteum, the patient exhibits a superficial vaso-dilatation accompanied by a severe, throbbing headache, The pain usually disappears with the fading of the visible vaso-dilatation within four or five minutes. The headache is probably the result of vaso-dilatation within the unyielding calvarium, and may be ascribed to the pressure on the meninges or the increased tension in the walls of the blood vessels themselves.

6. *Polyarthritis.* From the Mayo clinic[15] we are getting interesting reports of the results of ganglionectomies for polyarthritis. The cases usually present a pre-operative picture of cold extremities, marked sweating, tender and swollen joints, trophic changes in the muscles, skin and nails, combined with severe pain. Rowntree and Adson[15] comment that in this type of arthritis there is a hyperactivity of the sympathetic nervous system characterized by marked vascular disturb-

ances and sweating. Following operation these cases show surprising clinical improvement, perhaps the most striking feature being the relief of pain accompanying the improvement in circulation. The use of Brown's[16] "vaso-motor index" was based on the observation that the pain was less severe or absent, during fever when there was an improved circulation.

All of these observations, perhaps even the fact that arthritic patients experience variations in pain with changes in weather and altered barometric pressures, point to a relationship of the pain to vascular alterations. I am of the opinion that at least a part of the pain accompanying arthritis may arise in the walls of blood vessels.

DISCUSSION

Surgery directed toward a division or extirpation of portions of the visceral nervous system now commands a remarkable degree of interest. Peri-vascular sympathectomies, in spite of a lack of rational anatomical explanation, continue to yield favorable results in the hands of experienced operators; operations on the cervical sympathetics for angina pectoris; ramisections and ganglionectomies for spastic paralysis, pain of inoperable carcinoma, painful amputation of stumps, causalgia, Hirschsprung's disease, polyarthritis, Raynaud's disease and even certain cases of Buerger's disease and senile gangrene, are being reported in increasing numbers. In many of these conditions the major indication for surgery is the intractable pain, and, as Leriche[17] indicates, there is a definite field for this "Chirurgie de la douleur." As yet there is no unanimity of opinion as to the indication for operation, no standardization of technic and no agreement as to the underlying mechanisms responsible for the pain. It is my conviction that the blood vessels themselves are directly responsible for the pain in many instances.

When the time comes that we can state with assurance the rôle of the blood vessels in the causation of pain and disability for a given case, then surgery of this type will have a rational basis, whether directed toward the division of afferent neurons conducting pain impulses, or, more reasonably, toward division of autonomic fibers responsible for the functional abnormalities of the blood vessels. It would remain but to select the particular surgical procedure that most completely interrupts the visceral pathways to the affected part, with the least risk to the patient.

SUMMARY

Spasm and distention of smooth muscle in the walls of hollow viscera have been established as "adequate" stimuli for true visceral pain. The blood vessels exhibit these conditions in the same manner as the internal viscera and are provided with afferent pathways for the conduction of pain impulses. Experimental evidence is presented to

demonstrate that pain may arise from abnormal degrees of spasm or distention of the walls of blood vessels. Instances are cited illustrating surgical sensitiveness of arteries and conditions giving rise to pain in veins. A number of clinical syndromes characterized by pain are mentioned, in which afferent impulses of pain may originate in the walls of blood vessels.

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THE RELATIONSHIP OF AURICULO-VENTRICULAR CONDUCTION TIME IN RHEUMATIC FEVER TO SALICYLATE THERAPY*

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IN 1924, Cohn and Swift[1] emphasized the fact that the heart is frequently involved in patients with rheumatic fever. They found, upon electrocardiographic study of a series of such patients, that many of them exhibited an increased P-R interval (a prolongation in A-V conduction time) when compared with the basic normal P-R interval for that particular patient.

Levy and Turner[2] (1927) stated that the lesions which are responsible for prolongation of the conduction time may be influenced by antirheumatic drugs. These authors observed three patients with P-R time of .20 seconds or more and other signs of active rheumatic fever. Following the institution of salicylate therapy, in addition to the usual anti-symptomatic effects, there was a gradual reduction in the P-R time to within normal limits; and conversely there occurred a prolongation of the conduction time following withdrawal of the drug. A second course of salicylate was again followed by a shortening of A-V conduction.

Master[3] (1927) showed that salicylates administered in large doses to normal individuals had no effect whatsoever upon the A-V conduction time.

Cohn and Swift[1] (1924) "noticed in one patient in whom the conduction time was .24 on the sixteenth day of disease when the temperature was 103.5° F., that 4 days later, when the temperature had fallen to 100° F., a marked increase in its duration took place to the extent that dropped beats (incomplete heart-block) were observed. At this time she was taking neocinchophen.† It is inferred that neochinchophen was not responsible for this occurrence because of the fact that later, although the exhibition of the drug was continued, the conduction time fell to limits which, for this patient, were considered normal."

Carr and Reddick[5] (1928) in a study of conduction disturbances in acute rheumatic infections report that of the nine patients who developed A-V block while on sodium salicylate (4-8 gm. daily) eight patients showed a gradual return to normal A-V conduction time, while

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†The effects of cinchophen in rheumatic fever are precisely the same as those of salicylates.—Hanzlik[4].

the same dosage was continued; and the other retained the conduction disturbance long after discontinuance of the drug. Their observations led them to believe that the salicylates are without effect on conduction disturbances, neither causing them nor tending to control them.

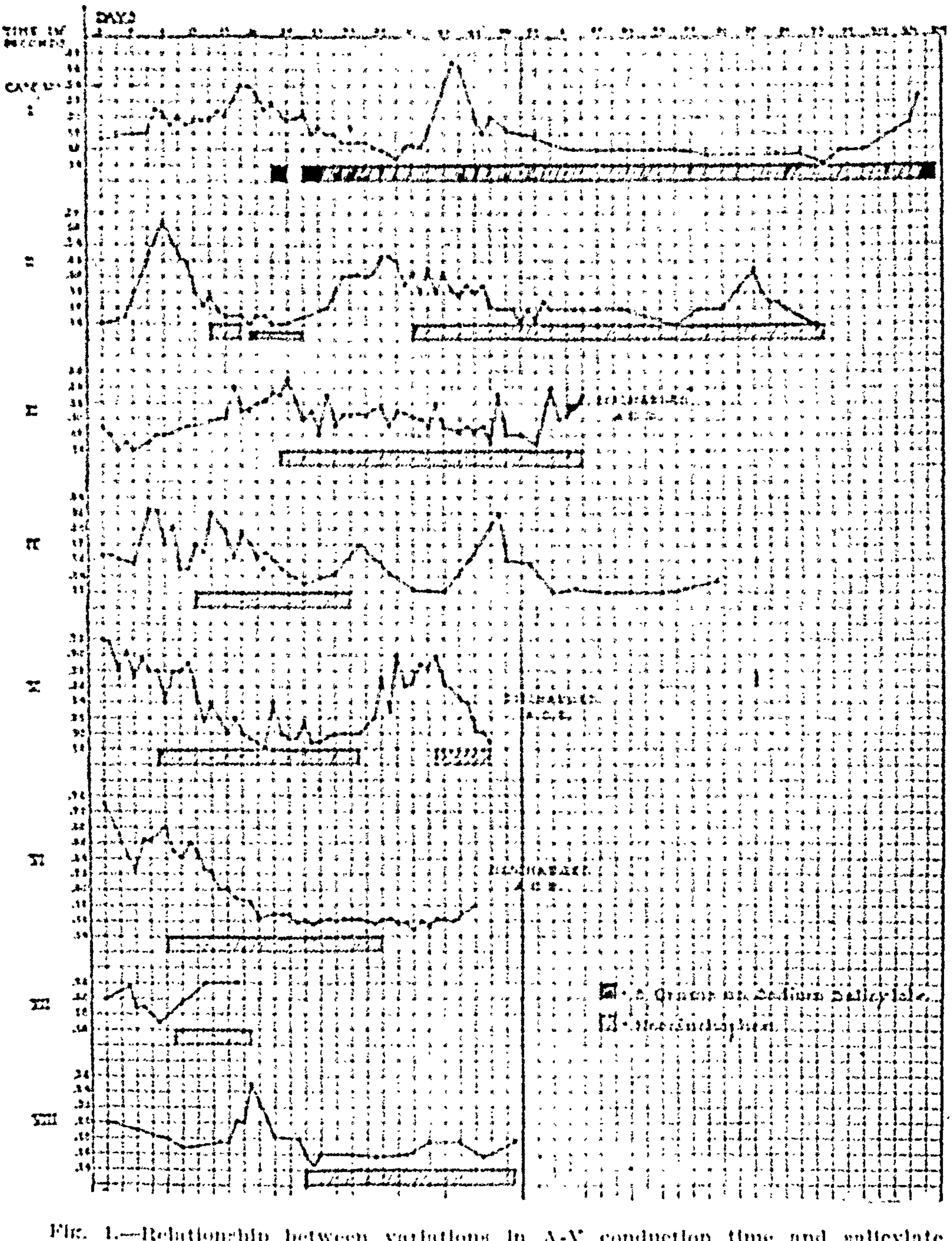

Fig. 1.—Relationship between variations in A-V conduction time and salicylate medication during the course of rheumatic fever. Time in days is plotted along the abscissa. The P-R interval in seconds is plotted along the ordinate.

In contrast to this, are the conclusions of Levy and Turner that "the administration of salicylate exerts a favorable effect upon the lesions in the heart muscle" as evidenced by the effect on A-V conduction time. Since this conclusion is of such far reaching significance and

has been challenged by Carr and Reddick, it was thought advisable to repeat this work upon a group of patients carefully controlled and observed for a long period of time.

METHOD

Every patient having rheumatic fever was electrocardiographed routinely twice a week. If any of these patients showed a P-R interval of .20 seconds or more, tracings were taken every day. Alternate

TABLE I

CASE NO.	AGE	SEX		DIAGNOSIS*
1	14	F.	A.	Rhematic fever, inactive and active
			B.	Enlarged heart, mitral stenosis and insufficiency, aortic insufficiency, acute myocarditis
			C.	Sinus tachycardia, auricular and ventricular premature contractions, first stage A-V block
			D.	Class II
2	18	M.	A.	Rheumatic fever (polyarthritis) active
			B.	Acute myocarditis
			C.	Normal sinus rhythm, first stage A-V block
			D.	Class II
3	34	M.	A.	Rheumatic fever (polyarthritis) active
			B.	Acute myocarditis
			C.	Normal sinus rhythm, first stage A-V block
			D.	Class II
4		F.	A.	Rheumatic fever (polyarthritis) active
			B.	Acute myocarditis and pericarditis
			C.	Sinus tachycardia, first and second stage A-V block
			D.	Class II
5	47	M.	A.	Rheumatic fever (polyarthritis) active
			B.	Acute myocarditis
			C.	Normal sinus rhythm, first and second stage A-V block
			D.	Class II
6	29	M.	A.	Rheumatic fever (polyarthritis) active
			B.	Acute myocarditis
			C.	Normal sinus rhythm, first and second stage A-V block
			D.	Class II
7	23	M.	A.	Rheumatic fever (polyarthritis) inactive and active
			B.	Enlarged heart, mitral stenosis, mitral insufficiency, aortic insufficiency, acute myocarditis
			C.	Normal sinus rhythm, first stage A-V block
			D.	Class II
8	32	M.	A.	Rheumatic fever (polyarthritis) inactive and active
			B.	Enlarged heart, mitral stenosis and insufficiency, aortic insufficiency, acute myocarditis
			C.	Sinus tachycardia, acute myocarditis, auricular premature contractions, first stage A-V block
			D.	Class II Peritonitis
9	24	M.	A.	Rheumatic fever (polyarthritis) active
			B.	Acute myocarditis, enlarged heart (x-ray)
			C.	Normal sinus rhythm, first stage A-V block
			D.	Class II

*Diagnosis conforms to the criteria adopted by American Heart Association.

cases showing increased A-V conduction time were given salicylates after a control period of one week. The dosage (8 grams per day) was just under the average toxic dose (10 grams per day) determined by Hanzlik.[4] That this was sufficient was evidenced by the fact that four patients showed toxic symptoms on this dose (cases 1, 2, 4, 5). Incidentally, all of the eight treated patients exhibited a prompt decline in temperature and alleviation of joint symptoms with the institution of salicylate therapy. The temperature stayed down while the patients

Table I—Cont'd

CASE NO.	AGE	SEX	DIAGNOSIS*
10	24	M.	A. Rheumatic fever (polyarthritis) active B. Acute myocarditis C. Normal sinus rhythm, first stage A-V block D. Class II
11	33	F.	A. Rheumatic fever (polyarthritis) active B. Acute myocarditis, acute pericarditis C. Normal sinus rhythm, first stage A-V block D. Class II
12	24	M.	A. Rheumatic fever (polyarthritis) active B. Acute myocarditis C. Normal sinus rhythm, first stage A-V block D. Class II
13	22	F.	A. Rheumatic fever (polyarthritis) inactive and active B. Enlarged heart, mitral stenosis and insufficiency, acute myocarditis C. Normal sinus rhythm, first stage A-V block D. Class II Acute sero-fibrinous pleuritis
14	44	M.	A. Rheumatic fever (polyarthritis) inactive and active B. Enlarged heart, mitral insufficiency, aortic insufficiency, acute myocarditis C. Normal sinus rhythm, first stage A-V block D. Class II
15	17	M.	A. Rheumatic fever (polyarthritis) inactive and active B. Enlarged heart, mitral stenosis and insufficiency, acute myocarditis C. Normal sinus rhythm, first stage A-V block D. Class II
16	20	M.	A. Rheumatic fever (polyarthritis) active B. Acute myocarditis C. Normal sinus rhythm, first stage A-V block D. Class II
17	47	M.	A. Rheumatic fever (polyarthritis) inactive and active B. Enlarged heart, mitral stenosis and insufficiency, acute myocarditis C. Normal sinus rhythm, first stage A-V block D. Class II
18	35	F.	A. Rheumatic fever (polyarthritis) active B. Acute myocarditis C. Sinus tachycardia, first stage A-V block D. Class II

*Diagnosis conforms to the criteria adopted by American Heart Association.

were taking the medication regardless of the variations in A-V conduction time. In Table I are listed the age, sex and diagnosis of all cases used for this study.

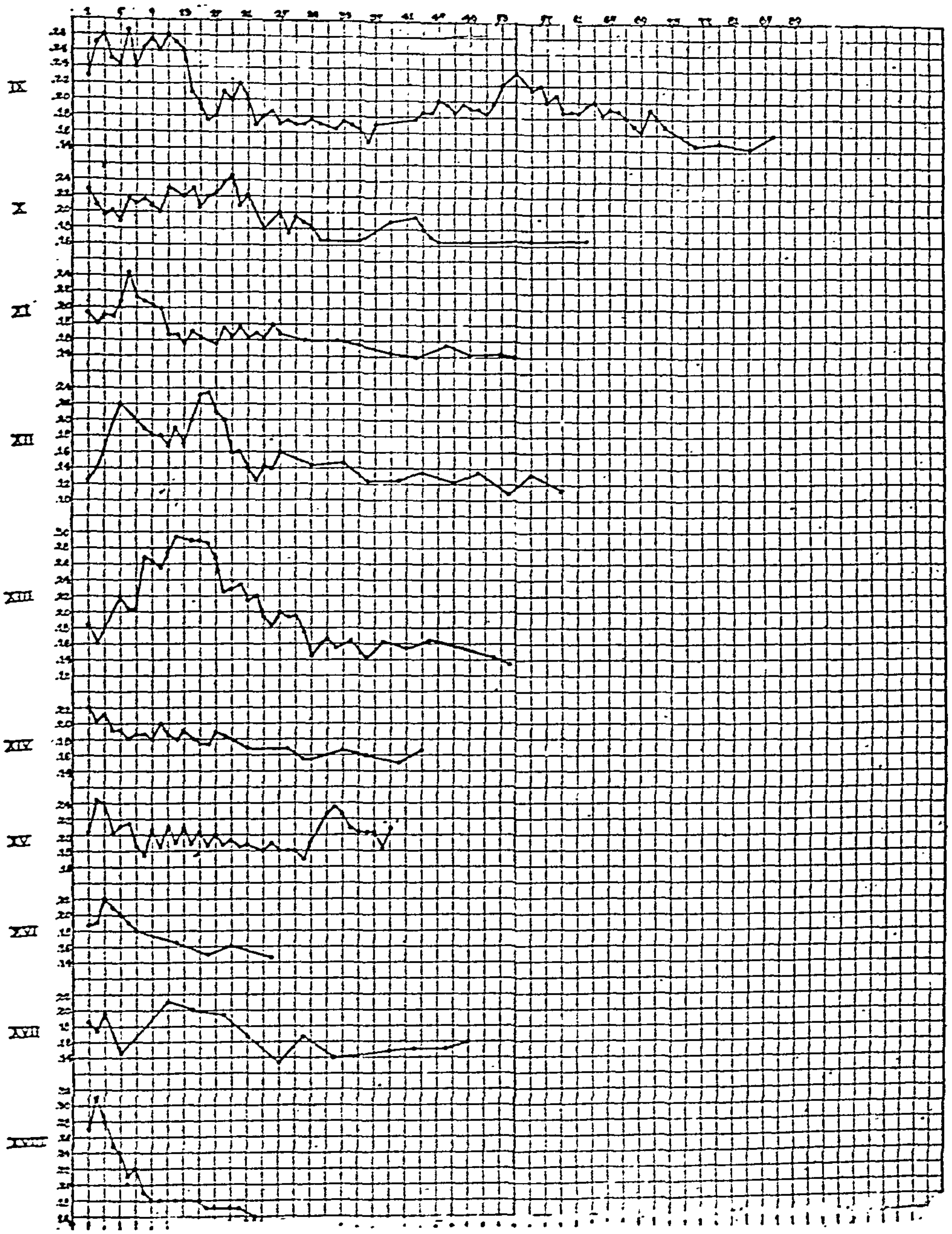

Fig. 2.—Variations in A-V conduction time during the course of rheumatic fever uncomplicated by salicylate therapy. Time in days is plotted along the abscissa. The P-R interval in seconds is plotted along the ordinate.

RESULTS

Eight patients were started on a daily dose of 8 grams of sodium salicylate following a control period of seven days after the discovery of an increased A-V conduction time. In figure 1 is plotted the rela-

tionship of variations in A-V conduction time to salicylate therapy. In two cases the P-R interval had already reached the normal for those patients before the medication was begun (cases 2 and 8). In cases 5 and 6 the P-R intervals gradually returned to normal while on salicylates. In case 5 the drug was discontinued and with this there was a subsequent increase in the P-R interval, which promptly fell to normal as the drug was resumed. This case was the only one among the eight which reacted in a manner similar to those reported by Levy and Turner. Incidentally even this case showed an increase in A-V conduction time while on the first course of salicylates. In contrast, four cases (1, 2, 3, and 7) definitely showed an increasing P-R interval while on salicylate medication. In cases 1, 2, 3, and 4 it is obvious that no relationship exists between changes in A-V conduction time and salicylate therapy.

In table 2 the variations in A-V conduction time from day to day are plotted in a control group of patients with rheumatic fever not receiving salicylate medication. A careful study of this chart shows that during the natural course of rheumatic fever uncomplicated by salicylate therapy there are wide and inconstant variations in the A-V conduction time. If antirheumatic drugs are used at any time during the disease it may easily be seen how at one time they might seem to cause an increase in A-V conduction time, at other times a decrease, and again to have no effect whatsoever. Thus if sodium salicylate had been given on the second day in case 18, when the P-R interval was .31 seconds, we would have been struck with the remarkable rapidity with which salicylates brought the A-V conduction time to within normal limits. Likewise, had salicylates been given on the second day of case 13 we should have been alarmed by the rapidity with which salicylates produced block.

CONCLUSION

Disturbances of A-V conduction time during the course of rheumatic fever show wide and inconstant variations, and there is no proof that they are influenced by salicylate therapy.

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THE VISUALIZED ESOPHAGUS IN THE DIFFERENTIATION OF LESIONS OF THE RIGHT AND LEFT HEART*

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HYPERTROPHY and dilatation confined to the right auricle and ventricle are most commonly caused by congenital defects such as patency of the ductus arteriosus, pulmonary stenosis, defects in the septa, or inversion of the large vessels. Any process such as chronic pulmonary emphysema, pulmonary fibrosis, or sclerosis of the pulmonary arteries, which produces obstruction or increased pressure in the lesser circulation, may likewise be a cause of right heart enlargement and failure. Although these conditions are far less common than lesions affecting the left heart, such as peripheral hypertension or disease of the aortic or mitral valves, they occur with sufficient frequency to make their recognition of some importance.

The clinical differentiation of congenital from acquired heart lesions is often difficult. This is especially true in those adult cases in which the history of heart disease since childhood is not clearly present, a history of rheumatism in some form is obtained, and there is little or no cyanosis. Given an adult with symptoms of heart disease, a history of rheumatism, an enlarged heart over the apex of which can be heard loud murmurs, and the diagnosis of acquired disease of the mitral valve is very likely to be made. If, in such a case, the teleroentgenogram or orthodiagraphic tracing shows an enlarged heart with a marked convexity of the left median curve representing a dilated conus pulmonalis, the diagnosis of mitral disease might appear to be amply confirmed.

This clinical and roentgenographic picture may, however, be due to a right heart lesion, either congenital in origin, or secondary to some disease affecting the pulmonary circulation. Obviously there are many diagnostic factors which must be considered and frequently the correct diagnosis is apparent by the usual clinical means. At times, however, as illustrated in the cases to be reported here, the clinical diagnosis may be very uncertain.

The postero-anterior roentgenogram which is obtained in these right heart lesions is occasionally difficult to differentiate from that obtained in mitral stenosis. In the typical cases, the high position of the median left convexity and the extreme enlargement of the conus pulmonalis may indicate the congenital origin of the lesion but in many cases the distinction is not so clear.

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There is one distinguishing feature, roentgenologically obtained, which has not been sufficiently emphasized in the past. In mitral stenosis the left auricle is the first cardiac chamber to enlarge and usually obtains a fairly large size before enlargement of the pulmonary artery or the right ventricle occurs. On the other hand, in most congenital lesions and always in cardiac enlargements of pulmonary origin, the hypertrophy and dilatation are confined entirely to the right side of the heart; the left auricle remains normal in size. This is a striking and constant difference between these two types of cardiac lesions and may be used to differentiate them with considerable accuracy.

As has already been repeatedly demonstrated, the best method of determining enlargement of the left auricle is by roentgenographic visualization of the esophagus.[1, 2, 3, 4, 5] The latter normally lies posterior to and in close contact with the left auricle. Enlargement of this chamber will always produce a distinct compression and posterior displacement of the esophagus. The technique and application of this method have been fully described by the author in a previous publication.[3]

The following cases are reported because they illustrate very aptly the application of this method and the remarkably accurate results which were obtained in a series of unusually difficult problems in cardiac diagnosis. The clinical findings in some of these cases will be reported in greater detail later and only those findings pertinent to the subject under consideration will be reported here.

CASE REPORTS

Case 1.—Left heart lesion; mitral stenosis. (From the Pediatric Service, University Hospital.) A girl of 11 years presented the typical symptoms of cardiac failure, a history of rheumatism, and the classical physical findings of mitral stenosis and regurgitation.

The teleroentgenogram of the heart (Fig. 1) showed marked enlargement with convexity of the left median curve, the appearance being typical of mitral valvular disease. The right lateral view with the barium-filled esophagus is shown in Fig. 2. There is a marked compression and posterior displacement of the esophagus in its middle portion extending down to a point about 3 cm. above the diaphragm. This corresponds to the location of the left auricle, is due to the massive enlargement of this chamber, and is characteristic of mitral disease. Clinical and Roentgenological Diagnosis: Cardiac enlargement, massive, mitral stenosis and regurgitation type.

This case is reported for contrast with the following and represents the typical findings in a left heart lesion.

Case 2.—Right heart lesion—pulmonary sclerosis. (From the Medical Service, University Hospital—private patient of Dr. Henry Ulrich.) A woman of 26 years presented a history of cardiac symptoms coming on suddenly after childbirth. These were progressive. On physical examination dyspnea, cyanosis, dilatation of neck vessels and pulsations over the chest were observed. An enlarged heart was made out, and over it a loud systolic murmur transmitted over the whole chest and back was heard. Evidences of pulmonary congestion and peripheral edema were present.

She was examined at different times by a number of clinicians. Two prominent cardiologists made the diagnosis of mitral stenosis. She was last seen by Dr. Henry Ulrich who made a clinical diagnosis of cardiac enlargement and failure probably from a congenital defect.

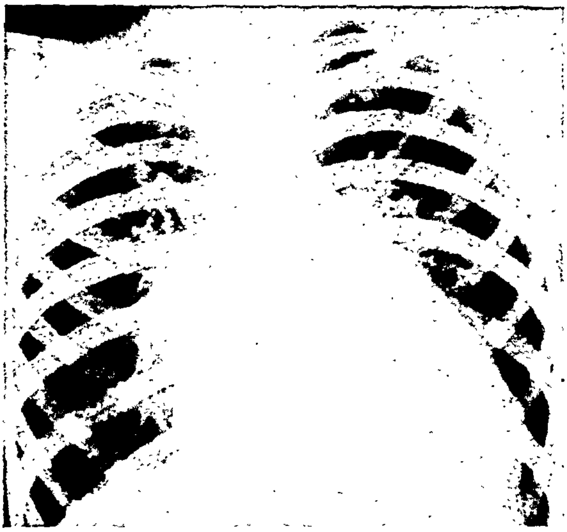

Fig. 1.

Fig. 2.

Fig. 1.—Case 1. Postero-anterior teleroentgenogram. Shows marked cardiac enlargement of the typical mitral type. Note bulging of conus pulmonalis (left median convexity).

Fig. 2.—Case 1. Right lateral view with barium-filled esophagus. Shows marked compression and posterior displacement of the esophagus in its middle third in the region of the left auricle. This indicates massive enlargement of the left auricle.

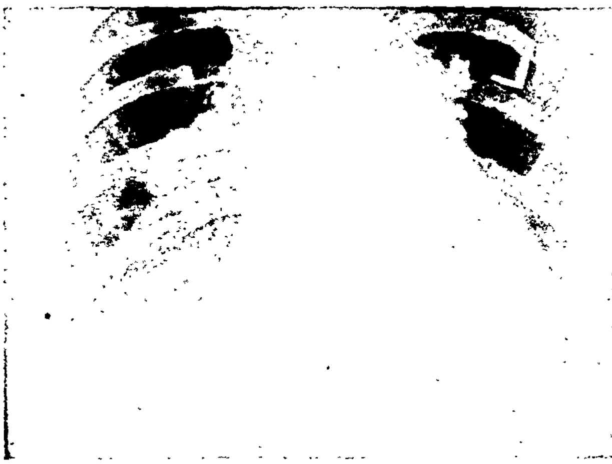

Fig. 3.

Fig. 4.

Fig. 3.—Case 2. Postero-anterior teleroentgenogram. Shows marked cardiac enlargement with extreme bulging of conus pulmonalis. Note high position and extreme convexity of left median curve. Note markedly dilated pulmonary vessels.

Fig 4.—Case 2. Right lateral view with barium-filled esophagus. Note the straight course without displacement or compression indicating no enlargement of the left auricle. Note space between spine and esophagus.

The teleroentgenogram (Fig. 3) shows a marked cardiac enlargement with extreme bulging of the left median curve representing a dilated conus pulmonalis. A notable dilatation of all the larger, and even some of the smaller, pulmonary vessels is shown, and on roentgenoscopic observation, a striking pulsation in these

vessels could be made out. The appearance is fairly characteristic of right heart enlargement but might be simulated by an extreme degree of mitral stenosis. Fig. 4 shows the right lateral view with the barium-filled esophagus. It will be noted that it runs straight through the thorax, shows no posterior displacement, and maintains its separation from the spinal shadow. This indicates the absence of left auricular enlargement, rules out conclusively mitral stenosis as a cause of such a marked cardiac enlargement, and confirms the impression of right heart enlargement, probably congenital.

Post-mortem examination was made by Dr. B. J. Clawson. The heart weighed 425 grams and showed marked hypertrophy confined to the right ventricle which was also much dilated. The other chambers and all the valves were normal; there were no congenital defects. The pulmonary arteries showed extreme arteriosclerosis with extensive dilatation. The lumina of many of the small arteries were almost closed. The other findings were of no importance.

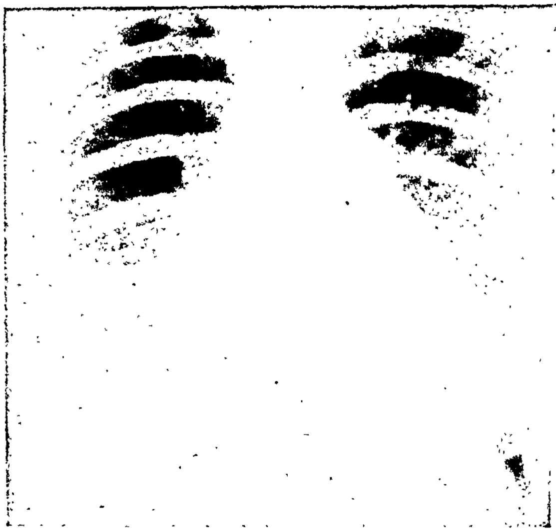

Fig. 5.

Fig. 6.

Fig. 5.—Case 3. Postero-anterior teleroentgenogram. Shows marked cardiac enlargement with extreme bulging of conus pulmonalis. Note high position and extreme convexity of left median curve.

Fig. 6.—Case 3. Right lateral view with barium-filled esophagus. Note the straight course without displacement or compression indicating no enlargement of the left auricle. Note space between spine and esophagus.

Various Clinical Diagnoses: (1) Congenital defect with cardiac enlargement. (2) Mitral stenosis with cardiac enlargement.

Roentgen Diagnosis: Right heart enlargement, probably congenital defect.

Post-mortem Diagnosis: Hypertrophy and dilatation right ventricle. Pulmonary sclerosis.

Case 3.—Right heart lesion—pulmonary hypertension? (From the Medical Service, University Hospital.) A woman of 24 years presented the clinical picture of cardiac failure coming on suddenly after excessive exertion. There was a doubtful history of rheumatism. Repeated peripheral edema was present but there were few signs of pulmonary congestion. Physical findings were variable. The heart was enlarged but murmurs were entirely absent at times, or only faintly heard and were not at all typical. Various clinical diagnoses were made including a definite diagnosis of mitral stenosis by two cardiologists.

The teleroentgenogram (Fig. 5) shows considerable cardiac enlargement with bulging of the left median curve. The high position and marked enlargement

of the conus suggests a congenital heart but the picture bears a close resemblance to that of marked mitral stenosis. Fig. 6 is the right lateral view with barium-filled esophagus which is quite normal. There is no left auricular enlargement, which ruled out mitral stenosis as a cause of the cardiac enlargement.

Post-mortem examination was made by Dr. W. A. O'Brien. There was a marked enlargement of the heart entirely confined to the right ventricle and right auricle. The remaining chambers were normal and the valves were normal; there were no congenital defects. The pulmonary arteries were dilated and showed some patches of sclerosis in the large branches. The smaller branches were, however, normal. The other findings were of no significance.

Various Clinical Diagnoses: (1) Mitral stenosis and regurgitation with cardiac enlargement. (2) Congenital defect and mitral stenosis with cardiac enlargement. (3) Congenital defect with cardiac enlargement. (4) Pulmonary sclerosis with cardiac enlargement.

Roentgen Diagnosis: Right heart enlargement, probably congenital defect.

Post-mortem Diagnosis: Right heart hypertrophy and dilatation. Possible pulmonary hypertension(?).

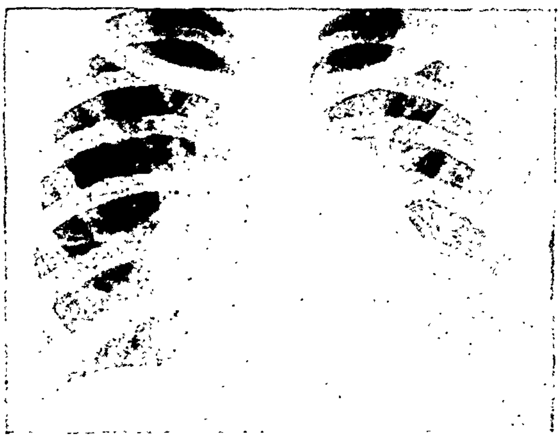

Fig. 7.

Fig. 8.

Fig 7.—Case 4. Postero-anterior teleroentgenogram. Shows marked cardiac enlargement similar to Fig. 1 and fairly characteristic of mitral disease of high degree. Note marked bulging of pulmonary conus.

Fig. 8.—Case 4. Right lateral view of esophagus. Shows slight displacement in middle third indicating very moderate left auricular enlargement. (Compare with Fig. 2.)

Case 4.—Right and left heart enlargement—mitral stenosis and absent interauricular septum. (From the Medical Service, University Hospital.)

A woman of 27 years presented the clinical picture of cardiac failure. Symptoms first began early in life following an attack of rheumatism and recurred frequently. The findings indicated both pulmonary congestion and peripheral edema. *Physical* findings showed a large heart of the mitral type, with a loud systolic murmur over the apex. Three clinicians disagreed as to the diagnosis as the physical findings were variable and difficult to interpret.

The teleroentgenogram (Fig. 7) shows a considerable degree of cardiac enlargement with marked bulging of the conus pulmonalis. The appearance is typical of either an extreme degree of mitral stenosis or a right heart enlargement of congenital origin. The right lateral view of the barium-filled esophagus (Fig. 8) shows only a small posterior displacement in the region of the left auricle (compare with Figs. 2 and 6) indicating only a very moderate enlargement of the latter. Considering the enlargement of the heart and the marked dilatation of the conus pulmonalis, the left auricle seemed disproportionately small if the whole process

were due to mitral stenosis. Accordingly (without any knowledge of the clinical findings) a roentgenologic diagnosis of mitral stenosis and a right heart lesion, probably a congenital defect, was made.

Post-mortem examination was made by Dr. W. A. O'Brien. The heart was markedly enlarged almost entirely on the right side. The left ventricle was, if anything, smaller than normal. The left auricle was moderately dilated and hypertrophied. The right ventricle and right auricle were massively enlarged. A high grade mitral stenosis probably of rheumatic origin was found. The interauricular septum was almost entirely absent. As a result the stenosis of the mitral valve affected the right auricle more than the left, the deficient septum preventing much increase in pressure in the left auricle. The right ventricle, however, responded to the double handicap of mitral stenosis and patent interauricular septum. The remaining findings were of little importance.

Various Clinical Diagnoses: (1) Mitral stenosis with cardiac enlargement. (2) Congenital defect with right heart enlargement. (3) Mitral stenosis with cardiac enlargement and possible congenital defect.

Roentgen Diagnosis: Mitral stenosis and congenital defect with enlargement of right heart and left auricle.

Post-mortem Diagnosis: Massive cardiac enlargement chiefly in right heart with moderate dilatation of left auricle. Mitral stenosis, probably rheumatic. Absent interauricular septum.

COMMENT

These four cases illustrate very well the possibilities of improved roentgen diagnosis of cardiac lesions with the aid of the barium-filled esophagus. A comparison of the postero-anterior films in all four cases shows a distinct similarity, while the films of the esophagus show marked differences under the varying conditions. The total heart size in Case 1, for example, is about the same as that in Cases 3 and 4. Yet in Case 1 there was marked esophageal displacement, in Case 3 no displacement and in Case 4 only slight displacement. These findings correspond perfectly with the respective sizes of the left auricle in these cases. In mitral disease (Case 1) with a fairly large heart we get extreme esophageal displacement and compression; in right heart lesions (Cases 2 and 3) no displacement; in combined mitral disease and congenital defects (Case 4) we get esophageal displacement which is far too small in proportion to the amount of cardiac enlargement.

The last three cases presented difficult diagnostic problems as indicated by the variety of clinical diagnoses. The close correspondence of the roentgen findings to the gross pathological findings is notable and indicates the accuracy of this method.

Thanks are due Dr. Henry Ulrich for the privilege of reporting the findings in Case 2.

SUMMARY

Four cases of cardiac disease are reported, in three of which post-mortem examinations were done and in the other of which the findings were unquestionable. These cases serve to illustrate the importance of the visualized esophagus in the differentiation of lesions of the right and left heart.

In a case of mitral disease the esophagus was displaced posteriorly and compressed by the enlarged left auricle.

In two cases of right heart enlargement from increased pressure in the pulmonary circulation the esophagus was not displaced indicating no enlargement of the left auricle.

In a case of mitral stenosis superimposed upon a congenital defect—absence of the interauricular septum—the esophagus was displaced slightly but much less than would be the case if the cardiac enlargement would have been due entirely to mitral disease.

The postero-anterior roentgenograms of the heart in mitral stenosis may resemble those of congenital and other right heart lesions closely. The visualized esophagus, in determining the presence or absence of left auricular enlargement, may aid greatly in making a correct diagnosis.

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THE "LATENCY THEORY" OF HEART-BLOCK AND INTERPOLATED VENTRICULAR PREMATURE BEATS*

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FOR more than twenty years there have been two opposing views which seek to explain the typical phenomena of partial heart-block. One, which may be termed the "latency theory," was proposed by Erlanger,[1] modified and developed by Straub[2] and Straub and Kleeman[3] and is at present held, in a different form, by Mobitz.[4, 5] According to this conception, the sinus impulse travels with normal velocity throughout the conducting tissues, but, upon reaching the junction between specialized tissue and ventricular muscle, the impulse produces a response of the ventricles only after a shorter or longer delay. The length of the delay is dependent upon the extent to which the ventricular muscle has recovered from the refractory state produced by its previous response and the strength of the impulse arriving by way of the junctional tissues. Damage in the A-V node or bundle was in general believed not to slow but to weaken the impulse. The theory, stated in this form, had to be abandoned when it was learned that an impulse, passing an injured region, will at once regain its normal strength in the undamaged tissue distal to the injury.

Mobitz[5] calls attention to the fact that the A-V node of the calf's heart consists of two portions, an auricular and a ventricular. Recognizing the difficulty in the theory as developed by Straub, he insists that the latency of the ventricular portion of the node determines the delay, and not the latency of the ventricular muscle. The sinus impulse arrives at this junction between the parts of the A-V node and, depending upon the excitability of the ventricular portion, the delay is longer or shorter.

The phenomena of partial heart-block with dropped beats as pictured by Mobitz[5] are illustrated in Figure 1. Sinus impulse *1* travels with normal velocity to the junction. After a slight latency the ventricular portion of the node lying just distally responds. The impulse then proceeds, with normal velocity, to the ventricles. The latency is short in this case because the previous beat was dropped and there has been a long recovery period. The width of the area in black may be taken as representing the duration of the absolutely refractory period of the

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tissue distal to the junction. Impulse *2* now arrives at a much earlier stage in the recovery of the ventricular part of the node. The P-R is, therefore, considerably longer. As will be readily understood from the figure, the consequence is that impulse *3* arrives at a still earlier phase of recovery and the latency is still greater. Impulse *4* arrives to find the ventricular portion of the node unresponsive and thus a beat is dropped. With impulse *5* the sequence of events begins again.

The opposing conception (Engelmann,[6] Lewis,[7] et al.) attributes delay to slow transmission through a depressed or injured region somewhere in the auriculo-ventricular pathway. It involves either the conception of a sluggishness in the response of successive muscular elements to the oncoming impulse or of a slow rise of action current strength to an effective intensity or both. But the conception does not admit of a single greatly exaggerated delay at one point. Too great a slowing would probably spell extinction of the impulse and the ventricular response would not occur. *This conception of partial block* has previously been described in some detail (Herrmann and Ashman[8]).

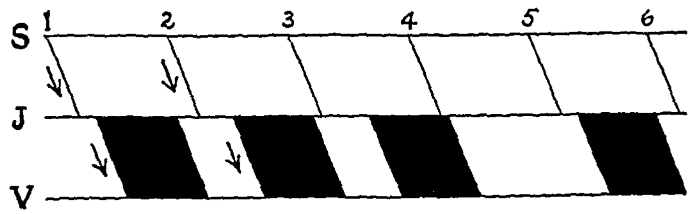

Fig. 1.—See text.

We now believe that certain details were perhaps insufficiently emphasized, while in other respects the presentation might have been simplified.

It should be pointed out that there is no intention of denying that latency at a single boundary may play a part in partial heart-block. Proof that it does so is lacking. On the other hand, there is good evidence that slow conduction is the important factor in the prolongation of the conduction time, if, in fact, it is not the sole factor.

It is not the purpose of this paper to attempt any further interpretation of partial block, but rather to present certain facts which demonstrate that the "latency theory" is not competent to explain all the observed phenomena.

Lewis[7] calls attention to a fact which he regards as in itself sufficient to rule out Mobitz' theory, namely, *that conduction through a* homogeneous strip of cardiac muscle is slowed by depression of any sort such as compression or increase in hydrogen-ion concentration. There is, therefore, no good reason to deny that depression caused by disease in the human heart cannot slow the impulse and lengthen the

P-R. Mobitz[5] admits that depression may slow intramuscular conduction, but argues that in partial block of the type represented there is no damage of the conducting pathway; that the effects are of vagus origin. Granting that this contention is correct, at least in many cases (e.g., over-digitalization), we must either advance other evidence against the "latency theory" or admit that it may be the correct one.

One of the first, and by no means the least formidable, of the difficulties encountered by the "latency theory" is the repeated observation of conduction times ranging from 0.5 sec. to as high, even, as 1.0 sec. (Thayer,[9] Herrmann and Ashman[8]). To explain why this is a difficulty, it is to be remembered that the action current associated with the response of each segment of muscle is generally regarded as the stimulus arousing the next successive segment to activity. When the impulse reaches the auricular portion of the A-V node and that portion responds, its action current does not continue to flow for more than about 0.3 sec. Variations in this duration depend upon the heart rate and other factors. In cases of greatly prolonged P-R intervals, therefore, according to the "latency theory," the ventricular portion of the node must respond to the stimulus from the more proximal portion anywhere from 0.1 to 0.6 sec. after the disappearance of the stimulating current.

Mobitz recognized this difficulty and was constrained to invoke some esoteric function of the nerve cells in the region of the A-V node. He is unable, however, to suggest how the nervous elements keep the stimulus going. Instead he falls back on the assertion that the typical phenomena of partial block are not obtainable in a strip of cardiac muscle where, of course, such special groups of nerve cells are not found. The answer to this assertion is that the typical phenomena of partial block *are* obtainable from strips of heart muscle.[15] Figure 2 is one of a number of examples obtained from transverse ventricular strips from the turtle heart, partial block between the ends having been induced by incisions near the center of the strip. The figure and legend are a sufficient explanation. This experiment does not, however, afford a complete refutation of the "latency theory" inasmuch as the action current at the one end of the strip had not died out at the time of response of the other end, and thus it is possible to argue that the delay represents a pause in Mobitz' sense.

Another phenomenon exhibited by the turtle heart amounts to practically crucial evidence against the "latency theory." Although there can be little doubt from the experiments of Lewis and Master[10] with the dog heart that the same behavior would be exhibited under similar conditions, the turtle heart is more suitable for experiment because its rate can be more easily controlled. Figure 3 is one example from among many. According to the usual convention, auricular beats are repre-

sented above, ventricular responses below. Abscissae represent time. Cycle lengths and P-R intervals are shown. The first series of beats (A), two in number, illustrate the well-known fact that when the recovery period is long the P-R interval is relatively short. P_1-R_1, pre-

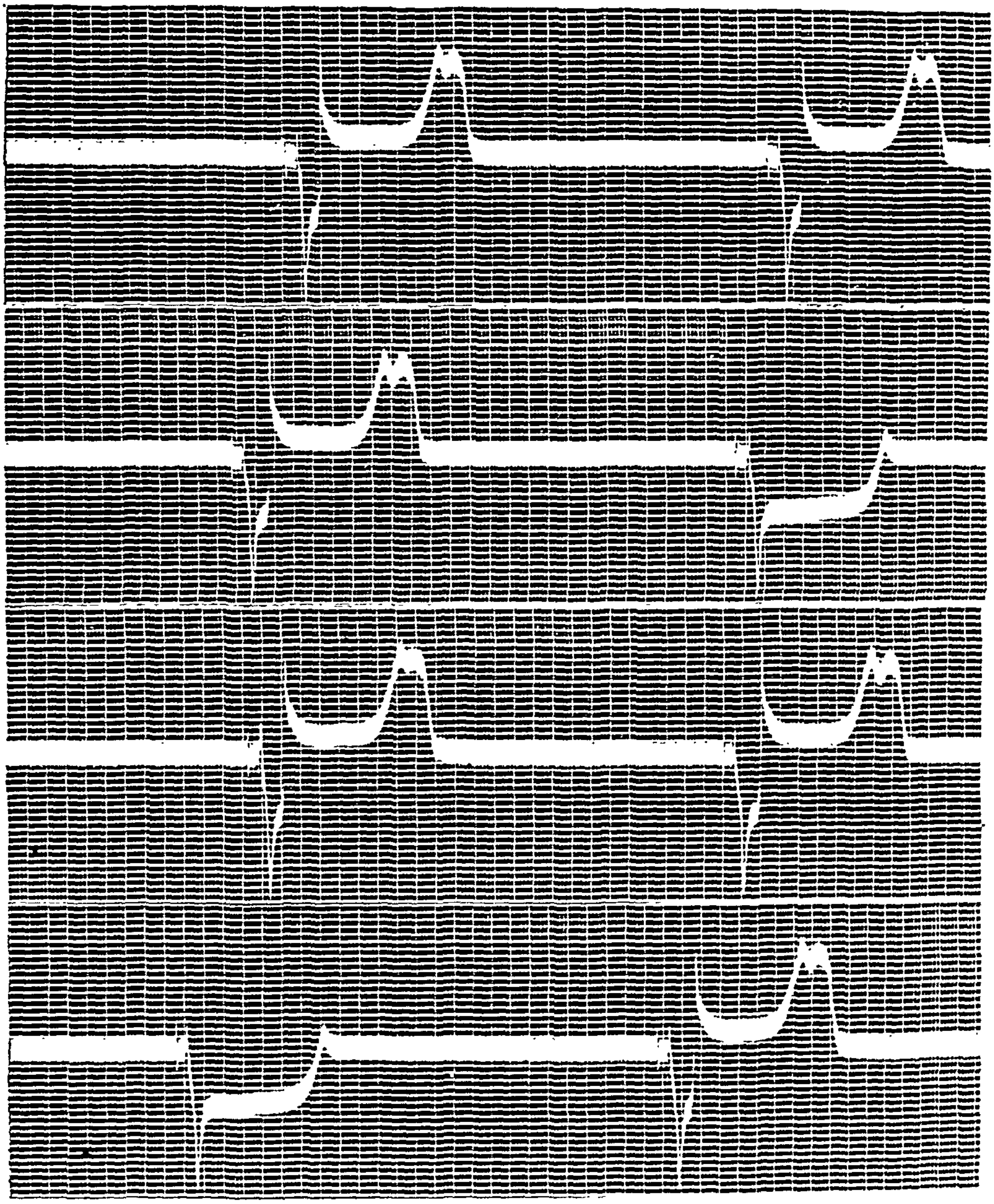

Fig. 2.—Continuous electrogram from transverse strip cut from turtle ventricle. Incisions had been made at the center of the strip leaving the two ends connected by a narrow bridge of tissue. Responses in every case are to break shocks applied to the right end of the strip. The response of this end is marked by the quick downward deflection; the response of the left end by the quick upward deflection.

The two responses, upper row, and the first response, second row, show progressive prolongation of the interval between the responses of the two ends leading up to block with the second response, second row. Following the blocked impulse the first conduction time is short (third row); the next interval is longer; the next (lower row) is blocked. Following this 2:1 block developed, but is not shown in the figure.

The time intervals in seconds between the successive responses of the right end of the strip and the ensuing conduction times (the latter in parentheses) are:

About 5.00 (0.20); 5.08 (0.224); 4.84 (0.24); 5.16 (blocked); 5.15 (0.217); 4.91 (0.24); 4.51 (blocked); 5.01 (0.23).

ceded by a rest of 10 sec., is 0.526 sec. P_3, after a 3.026 sec. rest, comes just before complete recovery in the conducting tissues and therefore P_3-R_3 is slightly prolonged (0.538 sec.).

What would have happened had another auricular impulse been interposed between P_1 and P_3? The consistent result of such interpolation is shown in the second group of responses (B). The blocked P has caused P_3-R_3 to increase from the expected 0.540 in this case to 0.652 sec., an increase of 21 per cent.

Thus an impulse, which according to Mobitz' view could not have caused a response of the structure in the turtle heart corresponding physiologically to the ventricular portion of the A-V node, did, nevertheless, greatly increase the conduction time (or "latency") for the following impulse. Now, it is well known that an ineffective stimulus does not prolong the refractory period of cardiac muscle. Consequently, it

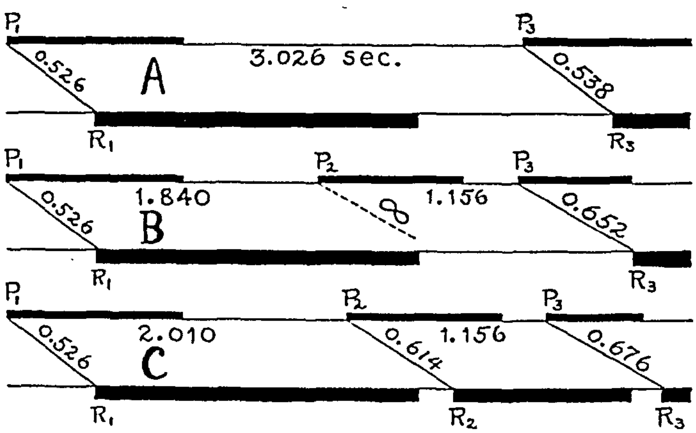

Fig. 3.—See text.

cannot be assumed that the blocked impulse affected the structures just distal to the plane of block. It was not a decrease in the excitability of these structures that was responsible for the prolonged P_3-R_3.

It may very justly be argued, however, that P_3 was weakened by the interpolation of P_2 and that this is the cause of the long P_3-R_3. In a sense, no doubt, that was true—P_3 was weakened. The long P_3-R_3 may, therefore, be due to the weakening and diminished effectiveness as a stimulus of P_3 and not to any change in the excitability of structures distal to the blocking plane of P_2.

The crucial test is to be seen in the lower group of responses (Fig. 3, C). Here P_2 is thrown in 2.01 sec. after P_1, just late enough to be transmitted. P_2-R_2 is quite long because of the short time allowed for recovery. Since the structures distal to the plane of blocking have responded, their excitability will be much lower when P_3 arrives than in the previous case where P_2 was blocked, and where P_2 cannot, therefore, be regarded as having invaded them. If Mobitz' conception is

the correct one, a P_3, thrown in at the same interval after P_2 as the P_2-P_3 interval in the second case, must either be blocked or else transmitted only after a much longer P_3-R_3 interval.

The actual result is seen in the figure. Following P_2, a P_3 is elicited at the time suggested. Therefore, the P_3 impulse will be weakened fully as much as in the former case.* Nevertheless, it will be observed that P_3-R_3 is now 0.676 sec., or only 3.7 per cent longer than it was when P_2 was blocked. Yet the structures distal to the plane of block, those corresponding functionally to the ventricular portion of the A-V node in the mammal, have had an estimated recovery period of but 0.18 sec. as contrasted with 1.23 sec. in the former instance.

The "*latency theory*" *which attributes all the delay (barring the* short conduction time proper) to latency in response of the structures distal to the plane of block, is manifestly unable to account for this result. For Mobitz to explain this result it would be necessary for him to make the highly improbable assumption that in partial block with constant auricular rate, latency plays the chief rôle, but that here, where block results from a change in auricular rate, *ventricular* latency has nothing to do with conduction time.

On the basis of the opposed conception, namely, that delay is due to slow conduction from element to element, the near equality of effect of the transmitted and blocked P_2 impulses is readily accounted for. It is only necessary to make the assumption that the blocked impulse traverses almost the entire length of the junctional tissues in which the slower conduction occurs. Thus the P_3 impulse following a blocked P_2 impulse will traverse nearly as great a stretch of relatively refractory muscle as it does when it follows a transmitted P_2 impulse. Its conduction time will, therefore, necessarily be nearly as great in the one instance as in the other.

Although, as already stated, Lewis and Master's[10] results indicate that similar relationships apply in all probability to conduction in the dog heart, yet this particular experiment was not done by them. Their results do show, however, that a blocked auricular impulse prolongs the conduction time for a following impulse, provided, of course, that the following impulse is not too late nor the blocked impulse too early. We thus possess for the dog a part, but not all, of the evidence against Mobitz' view which is so easy to obtain with the turtle heart.

Interpolated Ventricular Extrasystoles.—We have already referred to the fact that the phenomena of partial heart-block appear to be explicable without assuming the existence of an exaggerated pause at the

*Actually the weakening may be regarded as slightly greater, since the refractory phase of the muscle traversed by P_2 will in this instance be of slightly greater duration than in the former case. This follows from the fact that the P_1-P_2 interval is slightly longer than before. This fact counts all the more strongly against the "latency theory." In spite of the *greater* weakening of P_3 it goes through to the ventricle with an only slightly greater delay.

A-V junction. In interpolated ventricular premature beats, however, we generally meet with distinct, and often marked, prolongation of the P-R interval which follows the premature beat. This prolongation has been regarded by the protagonists of the "latency theory" as supporting their views.[2] For that reason we may here examine human electrocardiograms illustrating interpolated beats.

As is generally recognized, in order to explain interpolated ventricular beats at all it is necessary to suppose that the retrograde impulse from the ventricle is blocked at some point in its path back toward the auricle. Otherwise, it would cause an auricular response, or, if retrograde transmission were sufficiently slow, it would meet the oncoming auricular impulse in head-on collision. Were this latter event to occur, as it commonly does in premature beats, there would be no interpolation, since it is well known that impulses meeting on the same pathway cannot pass each other. There is mutual extinction.

Where does blocking of the retrograde impulse occur in interpolated premature beats? Briefly, it can hardly be at the junctions between ventricular muscle proper and Purkinje fibers because: (1) there is a transition in fiber structure at these junctions which presumably would make them unlikely as blocking points; (2) it is probable that the refractory period of the ventricular muscle is longer than that of the Purkinje fibers[7]; (3) one would expect the beat following the interpolated beat to be of definitely abnormal form. The last argument is particularly valid, for the prolonged P-R interval following the interpolated beat must be due to delay at and peripherally to the place where the previous retrograde impulse was blocked. If, as is usually the case, the interpolated beat arose in one or other ventricle, then, upon the arrival of the supraventricular impulse, one ventricle or region will be in a considerably more advanced stage of recovery than the other. This is a necessary consequence of the slow intramuscular conduction of the ectopic impulse. Therefore, the delay in response should be strikingly greater in one ventricle than in the other and aberrant complexes would necessarily result. Such aberration after interpolation is rarely observed. It is likewise improbable that the bundle branches are the region of blocking. Arguments (2) and (3) apply here also.

It follows, therefore, that blocking occurs either in the main stem of the bundle or within the A-V node itself. For convenience it is here assumed that the plane of block is somewhat below the middle of the node.

Figure 4 represents diagrammatically an interpolated ventricular premature beat and the supraventricular beat following it. In *A* the impulse is starting from a focus at *X* and beginning to spread through the Purkinje fibers. (See Legend.) The A-V node is represented as not yet recovered from the absolute refractory state associated with

its previous response.* In *B* the impulse spreads throughout the left ventricle, and thus the invasion of the ventricles continues until in *E*, after 0.12 sec., both ventricles have been invaded and the retrograde impulse becomes blocked low in the A-V node.† In *F*, 0.10 sec. later, an impulse starts from the sinus node. In *G* the auricles are being invaded, while the left bundle branch has recovered from its absolutely refractory state and is now relatively refractory, strongly so near the

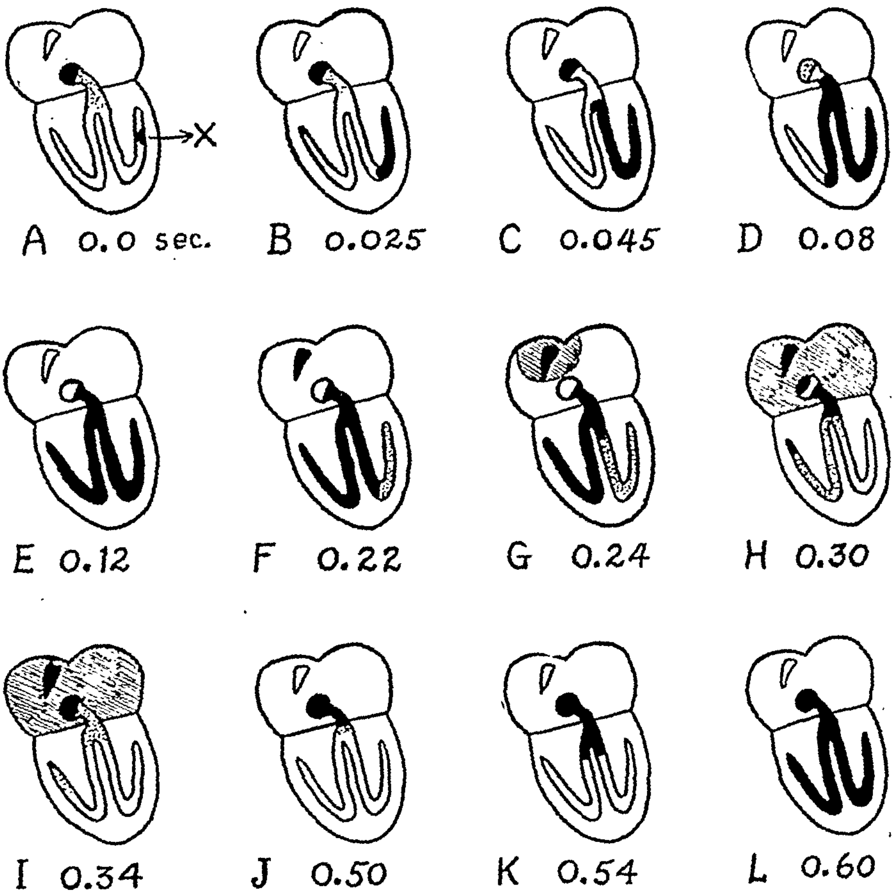

Fig. 4.—Successive stages in the invasion of the ventricles by the interpolated ventricular premature beat and by the following sinus impulse. In each diagram, the auricles are shown above, the ventricles below. The S-A (above) and A-V nodes are represented in the auricles; the A-V bundle extends from A-V node down into the ventricles where it bifurcates. No attempt is made to represent changes in the ventricular muscle proper.

Black signifies absolute refractoriness; stippled areas are relatively refractory; white areas, non-refractory.

Time from beginning of ectopic beat is shown below each heart. The velocity of spread of the impulse and other time relations are largely inferred; they are not in all cases directly determinable from the electrocardiogram. For description, see text.

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*The moot question as to whether premature beats arise from a regularly or occasionally automatic focus or result from a circus contraction does not at all influence the argument.

†It is possible to estimate the time ordinarily required for a free-wall ventricular ectopic impulse to travel from its point of origin back to the bifurcation of the bundle. This was done by examining a number of electrocardiograms exhibiting interference between ordinary premature and supraventricular impulses. Such "combination" complexes (Wilson and Herrmann[11]) cannot occur if the retrograde impulse reaches the bifurcation before the supraventricular impulse. While recognizing that retrograde time to the bifurcation will vary with the position of the ectopic focus, with the degree of prematurity, and with the condition of the muscle, yet the average time may be taken as not more than 0.05 sec. Thus the time for retrograde transmission to the A-V node may reasonably be regarded as not more than 0.11 or 0.12 sec. Retrograde conduction to the auricles in other cases affords additional information.

bifurcation. *H* shows the further retreat of refractoriness in the ventricles, completion of invasion of the auricles, and represents invasion of the A-V node as well advanced. In *I* the retreat of absolute refractoriness is complete, and the sinus impulse has just reached the plane of retrograde block. The main bundle is still strongly relatively refractory and for that reason conduction through it is extremely slow (Drury and Regnier[12]). *J*, *K*, and *L* show the further normal invasion of the ventricles by the supraventricular impulse.*

It should be noted that from *E*, when the retrograde impulse was blocked, to *I*, when the sinus impulse arrives at the plane of block, an interval of 0.22 sec. is inferred to have elapsed. Although short, this is probably not too short a time for recovery from the absolutely refractory state in case of a response terminating as short a diastolic rest period as that preceding the premature beat. Experimental evidence for this statement will appear in a forthcoming paper by the author.

We must not at once conclude, however, that by showing conduction without a pause to be possible we have ruled out the pause. In fact, a possible difficulty presents itself. The supraventricular impulse (*I* to *K*) is regarded as advancing into tissue, each successive invaded segment of which has had a longer time for recovery from its strongly relatively refractory state. This is true, not only because the direction of conduction is now opposite to that of previous invasion by the retrograde impulse, but also because delay in conduction in the tissue traversed gives additional time for recovery of the tissue lying in advance of the active segments.

The question, therefore, arises as to whether we should expect as great a prolongation of the P-R interval following the interpolated beat as is actually observed to occur. In answer to this question, it may be pointed out that the example chosen for illustration in Figure 4 presents nearly as great a prolongation as any case found in the series examined. In one case the prolongation is considerably greater, but in this there was a disturbance in conduction which rendered it unsuitable for illustrative purposes. The P-R increased from 0.21 sec. to a maximum of about 0.43 sec. In the example illustrated in the figures, the increase is from a normal P-R of 0.19 to one of 0.32 sec. Other cases show increases of from 0.17 to 0.215 sec.; from 0.13 to 0.19; from 0.17 to 0.325; from 0.13 to 0.18; and from 0.14 to 0.19. It is clear throughout the series of electrocardiograms that the earlier the P-wave falls

*The reader may have detected an apparent inconsistency in our argument. Why is it, if, as illustrated in Figure 4, one ventricle recovers later than the other, aberration of the ventricular complex following the interpolated beat does not occur? The answer is to be found in the delay in the node and main bundle which gives all the more quickly recovering tissues below ample time for recovery? As a matter of fact some of the beats in question do show a barely perceptible deviation from the normal, a change hardly great enough to be called aberration, and not nearly so great as would be anticipated if, as discussed above, retrograde block and the observed P-R increase depended upon retrograde block of the ectopic beat in the ventricles.

with reference to the T-wave of the interpolated beat, the longer is the P-R interval. If too early, blocking occurs and the premature beat is not interpolated. It is usual to find both interpolated and ordinary non-interpolated beats in these cases.

It cannot be too strongly stressed that if the interpolated beat be of junctional origin, i.e., from a focus near the retrograde blocking point, the prolongations may be greater, and it must also be kept in mind that, because of the likelihood of aberration of very early junctional prematures, it may be impossible to distinguish them from ventricular premature beats. In such a case the ectopic impulse is not retrograde, and while the supraventricular impulse is invading the bundle there will not have been as long a time for recovery in the successively invaded segments. In such a case, too, a P-wave arising as early as in the interval between R and T may be transmitted under favorable circumstances. On the other hand, in the cases examined, where the premature beat is of strictly ventricular origin, such early impulses have invariably been blocked.

One further point may be touched upon, i.e., why is the retrograde impulse blocked? On this point we can say nothing. Equally premature impulses in some hearts may pass back to the auricles. One thing, however, seems certain and has been long recognized. Retrograde block in interpolated beats is not contingent upon damage of the conducting pathways. Nor can it be assumed that separate pathways are involved in forward and retrograde conduction (Skramlik[13]), one of which is injured. In this connection a recent paper by Ashman and Hafkesbring[14] is pertinent.

SUMMARY

Experimental evidence has been presented which shows that the fundamental postulates of the "latency theory" of partial heart-block are not valid for conduction in the turtle heart.

From an examination of interpolated ventricular premature beats it is concluded that the observed phenomena do not compel us to accept that theory for the human heart.

The author is greatly indebted to Dr. G. R. Herrmann for permission to examine and make use of the more than four thousand electrocardiograms in the Heart Station at Charity Hospital and for helpful comment upon the text of this communication.

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DIPHTHERIA AS A CAUSE OF LATE HEART-BLOCK*

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THE occurrence of unexpected cases of heart-block in otherwise healthy persons and especially the occasional instance in a child or young adult suggests that there must be some other causative factors besides arteriosclerosis, syphilis and rheumatic fever. Years ago syphilis in the form of gumma of the septal tissue was thought to be a frequent cause, and rarely gummas have been recorded, but not in nearly sufficient numbers to account for even the majority of cases of heart-block. It is undoubtedly true that arteriosclerosis is a contributing and perhaps the most important single causative factor in the majority of cases, but a number of patients, recently seen by us, in whom arteriosclerosis was conspicuous by its absence and in whom there was no evidence of syphilis, coronary artery disease, or rheumatic infection, and where there was no other obvious influence such as digitalis or fever, have led us to look farther for etiological factors. Some years ago mention was made by one of us[1] in a footnote that in several cases of Adams-Stokes disease there had been a history of early diphtheria. For this reason a study has been made to determine the incidence of a history of early diphtheria in patients with heart-block or Adams-Stokes disease.

This concept of causal relationship gains theoretical support from the pathological findings in diphtheria. Marvin and Buckley[2] described two cases of diphtheria which developed complete heart-block, as proved by electrocardiograms, during the course of the disease. In one case microscopic sections of the conduction apparatus showed edema and infiltration about the bundle of His, including both branches, as well as about the sino-auricular and auriculo-ventricular nodes. McCulloch[3] reported three proved cases of complete heart-block during diphtheria. Fleming and Kennedy,[4] Magnus-Alsleben,[5] Parkinson,[6] Price and Mackenzie,[7] Röhmer,[8] and Schwensen[9] have each reported one such case. Korak[10] recently has described two cases of Adams-Stokes disease following diphtheria. However, Jones and White,[11] in a follow-up study of 100 cases of diphtheria over a period of not longer than five to eight years, failed to find heart-block in a single case. It is our belief, however, that diphtheria may influence the onset of heart-block many years after the occurrence of the original infection. We feel that had the 100 cases studied by Jones and

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White been followed 20 or 30 years longer, instances of heart-block might have been found. It must be remembered also that, while diphtheria is a relatively common condition, heart-block is rare, and the combined association would necessarily be infrequent. Nor should it be thought that subsequent heart-block need be a common late sequel of diphtheria.

Cases for this study were selected so that only those were included in which the diagnosis of heart-block was proved by electrocardiograms, and in which there was a definite statement in the past history as to whether the patient had or had not had diphtheria in childhood. No cases were included in which this latter question was uncertain. In this regard a recent experience in questioning a patient in the hospital wards is of some interest. The patient was suspected of having heart-block and the routine clinical record gave a negative past history for diphtheria. However, when the direct question was asked by one of us the patient admitted having had severe diphtheria with post-diphtheritic paralysis in childhood and stated that she had not been asked the direct question previously. A positive history, therefore, in our series is definitely positive and comparatively reliable, and some of those routinely reported negative also may have been positive. No patients were included that had been taking digitalis recently. Similarly all cases with a past or present history of coronary occlusion were excluded as well as those suffering from acute rheumatic heart disease. Although it was not intended to include cases having other acute febrile conditions at the time when heart-block was present, none was found. The purpose of this method of choice was to study those cases of heart-block which were otherwise inexplicable.

With these limitations 20 cases taken from the records of the Peter Bent Brigham Hospital and from those seen in private practice were available for study. There were 14 cases of complete heart-block, five of partial block and one which varied from partial to complete block during the period of observation. In all but one the block was permanent. Ten patients had Adams-Stokes syndrome. No case happened to have a syphilitic history or a positive Wassermann reaction.*

The striking fact that came out of this study, as shown by the accompanying table, is that 10 of the 20 cases of inexplicable heart-block or 50 per cent, gave a positive past history of diphtheria. Despite the fact that diphtheria is a common condition, this cannot be an accidental relationship, for a routine questionnaire in 600 consecutive surgical case histories disclosed a positive incidence of diphtheria in only six per cent. There must, therefore, be some element of cause and effect. It is also interesting that the average age of the ten cases that did have

*Since the completion of this report four additional patients having otherwise inexplicable heart-block have been seen by us. Three of them gave a history of having had diphtheria in childhood.

TABLE I

NO.	CASE NO.	SEX	AGE	DIAGNOSIS	VENTRICULAR HEART RATE	BLOOD PRESSURE	WASSERMANN	PAST HISTORY	YEARS SINCE DIPHTHERIA
1.	10,942	f	17	Heart-block, partial. Aortic and mitral insufficiency.	50	120/40	neg.	Diphtheria, severe, at five. Pyelitis at eleven.	11
2.	11,593	f	50	Heart-block, complete. Adams-Stokes disease. Hypertension. Chronic nephritis.	30	190/60	neg.	Diphtheria at eight. Scarlet fever.	42
3.	15,906	f	61	Heart-block, complete. Auricular fibrillation.	40	176/64	neg.	Diphtheria.	50
4.	17,575	m	61	Heart-block, complete. Auricular fibrillation.	30	160/50	neg.	Diphtheria as a child.	50
5.	19,934	m	66	Heart-block, complete. Pernicious anemia. Aortic insufficiency.	40	130/40	neg.	Diphtheria as a child. "Rheumatic gout."	55
6.	19,294	m	50	Heart-block, partial. Chronic arthritis.	60	142/66	neg.	Diphtheria. Pneumonia as a child.	51
7.	22,182	m	32	Heart-block, complete. Adams-Stokes disease.	30	122/55	neg.	Diphtheria, severe, at nine. Asthma at eight.	23
8.	22,720	f	52	Heart-block, complete. Adams-Stokes disease. Cholelithiasis.	30	175/70	neg.	Diphtheria, severe, at six and seven. Paralysis of legs following.	45
9.	25,859	m	28	Heart-block, complete. Ulcer, duodenal.	43	120/60	neg.	Diphtheria, twice. Pneumonia as a child.	18
10.	34,929	f	59	Heart-block, complete. Adams-Stokes disease. Hypertension. Cholecystitis, chronic.	34	190/70	neg.	Diphtheria, severe, at twelve (pulse very slow and feeble, difficulty in walking for one year).	47
11.	9,961	f	64	Heart-block, complete. Adams-Stokes disease. Hypertension.	35	200/122	neg.	Not sure about diphtheria.	
12.	10,061	m	46	Heart-block, partial. Adams-Stokes disease.	35	170/90	neg.	Typhoid only.	
13.	5,458	m	84	Heart-block, partial. Chronic nephritis. Hypertension.	37	220/110	neg.	Negative.	

TABLE I—CONT'D

NO.	CASE NO.	SEX	AGE	DIAGNOSIS	VENTRICULAR HEART RATE	BLOOD PRESSURE	WASSERMANN	PAST HISTORY	YEARS SINCE DIPHTHERIA
14.	15,035	f	72	Heart-block, variable. Adams-Stokes disease. Aortic insufficiency. Hypertension.	40	220/66	neg.	Negative.	
15.	27,035	m	36	Heart-block, complete. Adams-Stokes disease. Congenital heart defect (septum defect).	40	115/60	neg.	Negative.	
16.	28,081	f	65	Heart-block, partial. Adams-Stokes disease. Chronic myocarditis. Hypertension.	45	190/60	neg.	Scarlet fever.	
17.	28,663	m	64	Heart-block, complete. Hypertension.	35	190/70	neg.	"Rheumatism" (no redness and swelling of joints).	
18.	30,786	m	21	Heart-block, complete.	34	124/50	neg.	Infection of foot 6 weeks before, followed by slow heart.	
19.	32,935	m	75	Heart-block, complete. Myocardial insufficiency (congestive). Nephritis, chronic.	30	156/100	neg.	Influenza.	
20.	33,788	m	59	Heart-block, complete. Myocarditis, chronic. Hypertension. Cirrhosis of liver.	35	200/75	neg.	No previous infections.	

SUMMARY

	PATIENTS WITH POSITIVE DIPHTHERIA HISTORY	PATIENTS WITH NEGATIVE DIPHTHERIA HISTORY
Average age, years	47.6 (17 to 66)	58.6 (21 to 84)
Blood pressure, average	153/58 mm.	192/66 mm.
Ventricular heart rate, average	38	37
Average number of years since diphtheria	39 (11 to 55)	

diphtheria was 11 years less than that of the ten that did not. One might infer from this that in the younger patients the previous diphtheria has a greater significance than in the older, and that in the latter group the more customary factor of arteriosclerosis plays the primary rôle. This is well borne out by the fact that the older group without diphtheria had an average systolic blood pressure 40 mm. higher, and an average diastolic pressure 11 mm. higher than those with a past history of diphtheria.

It must be remembered that heart-block itself with the resulting bradycardia and long diastolic pauses of the heart, produces a slight elevation in the systolic and lowering in the diastolic blood pressures. The readings in our cases, therefore, need to be interpreted with this in mind. Thus the group with a positive history of diphtheria, having an average blood pressure of 153/58, may be regarded as having an essentially normal blood pressure level.

Our interpretation of these data is that diphtheria in some way, after a variable latent period, either brings about the impairment in the conduction apparatus as the sole cause of the heart-block, or predisposes the heart to the insidious process of sclerosis which in the absence of diphtheria would have matured at a later age.*

The following three case reports serve to illustrate the type of material with which we are dealing. Two of the patients were young people having normal blood pressures who had complete heart-block with no demonstrable cause except a history of severe diphtheria in childhood. The other was a woman of 52 years characteristic of the older group.

CASE HISTORIES

Case 7.—Medical No. 22182. A white man, 32 years of age, entered the hospital on October 15, 1923, complaining of slight dyspnea on effort and dizziness for nine months, and in the last two days two attacks of unconsciousness, each lasting about five seconds. His past history revealed "asthma" at eight years and severe diphtheria at nine. His heart rate was 30 and regular. Blood and urine examinations were negative. Blood Wassermann reaction was negative. Vital capacity was 3950 c.c., which was normal. Blood pressure was 122/50 mm. of Hg. Electrocardiograms showed complete heart-block and defective intraventricular conduction. Physical examination showed the heart to be slightly enlarged. A faint systolic murmur was heard at the apex. No diastolic murmur was present. Auricular beats were audible over the precordium and visible in the neck. The diagnosis of Adams-Stokes disease and complete heart-block was made. Vagal pressure, ocular pressure, atropine sulphate gr. 1/30 (0.002 gm.), digitalis folia 2.6 gm. were tried without symptomatic relief or change in the electrocardiographic tracings. Finally barium chloride gr. ½ (0.030 gm.) four times a day by mouth and adrenalin chloride, 1.0 c.c. of a 1/1000 solution subcutaneously 30 minutes after each dose of barium, were given with complete and permanent relief. He has now been entirely free

*A further possibility arises in this connection, i.e., that early diphtheria may be related in a similar causative manner in some of the cases of so-called chronic myocarditis which do not have heart-block hypertension, valvular disease, coronary artery disease and the like.

from symptoms for six years. He took barium chloride for only two weeks. At no time during his stay in the hospital did he have fever.

CASE 8.—Medical No. 22720. A white woman of 52 years was admitted to the hospital December 31, 1923, with the complaints of attacks of fainting and complete unconsciousness increasing in frequency and severity for the last five years. During an attack her pulse could not be obtained and immediately after the attack the rate was 30. She had twice injured herself by falling and on the day before admission had lost control of rectal and bladder sphincters during an attack. She had measles, mumps, whooping cough and scarlet fever as a child. She had diphtheria twice at the ages of six and seven years. Following the second attack there was some paralysis of both legs so that she could not walk for one year. For the last few years she had attacks of pain in the right upper quadrant of the abdomen so severe as to require morphia and strongly suggestive of gall stone colic. The temperature and respiration were normal, the pulse 30 and regular. The blood pressure was 175/70 mm. The blood count and hemoglobin were normal. The Wassermann reaction was negative and she gave no history of syphilis. Kidney function and urine were normal. Electrocardiograms showed complete heart-block with an auricular rate of 50 and a ventricular of 30. The heart was moderately enlarged. The sounds were of good quality. There was a loud harsh systolic murmur over the aortic area but no thrills. No diastolic murmurs were heard. Distinct auricular waves were to be seen in the veins of the neck. During her stay she had three attacks of unconsciousness when no ventricular beat was audible for from 20 to 30 seconds. On the 15th day she began to take barium chloride gr. ½ (0.030 gm.) by mouth three times a day and left the hospital fifteen days later, having had no attacks since the commencement of the barium. The diagnosis was Adams-Stokes disease, complete heart-block and cholelithiasis.

CASE 9.—Medical No. 25859. A white man, 28 years old, entered the hospital on May 14, 1925 complaining of pain in the chest for two years without dyspnea or other evidence of cardiac disease, and epigastric distress typical of peptic ulcer of five years' duration. At the ages of 12 and 13 he had had two severe attacks of diphtheria. His past history was otherwise negative except for measles and whooping cough as a child. His heart was regular with a rate of 43. His blood pressure was 120/60 mm. Electrocardiograms showed complete heart-block, the auricular rate being 63 and the ventricular rate 43. The heart was not enlarged. There were no murmurs except a soft blowing systolic over the base. There was a third sound in some cycles thought to be the auricular beat. The vital capacity was 4150 c.c. or 108 per cent of normal. Blood and urine were entirely negative. He was treated for his ulcer with Sippy management and returned home improved, with the diagnosis of complete heart-block and duodenal ulcer.

SUMMARY

A group of twenty patients having proved heart-block without the customary causes such as coronary artery disease, digitalis, fever and rheumatic infection were studied to determine the incidence of diphtheria in childhood. The incidence was 50 per cent as compared to six per cent in 600 consecutive control surgical cases. The average age of patients with a positive diphtheria history was 11 years younger and their systolic blood pressure 40 mm. lower than was the case with those with a negative history.

Diphtheria in childhood appears to be an etiological factor in the development of heart-block in later years.

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THE DISTRIBUTION OF THE POTENTIAL DIFFERENCES PRODUCED BY THE HEART BEAT WITHIN THE BODY AND AT ITS SURFACE*†

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ESSENTIALS OF EINTHOVEN'S TRIANGLE

In 1913 Einthoven, Fahr, and de Waart[5] made an extremely important contribution to the subject of electrocardiography. They described a method by means of which it is possible to determine the direction and the "manifest value," or in other words the value manifest or effective in the three standard electrocardiographic leads, of the potential difference produced by the heart beat at any given instant in the cardiac cycle.

This method is now well known to all students of electrocardiography; nevertheless the principles upon which it is based, and consequently the limitations to which it is subject do not appear to be generally appreciated. Having myself entertained at one time a number of erroneous ideas regarding it, from which I have freed myself only gradually and with much trouble, it seems worth while to give a brief account of my own difficulties in order that they may be avoided by others, and in order to point out that the fundamental principles involved have important applications in many electrocardiographic problems.

Einthoven's original description of the method is a masterly one. All of the assumptions upon which it is based are clearly stated; the method is applied in the solution of several problems, and its use is fully illustrated. It must be remembered, however, that Einthoven was thoroughly familiar with electrical theory and with mathematical physics; he spent most of his life working on problems that required an extensive knowledge of these subjects. Most electrocardiographers, on the other hand, are neither mathematicians nor physicists. Conse-

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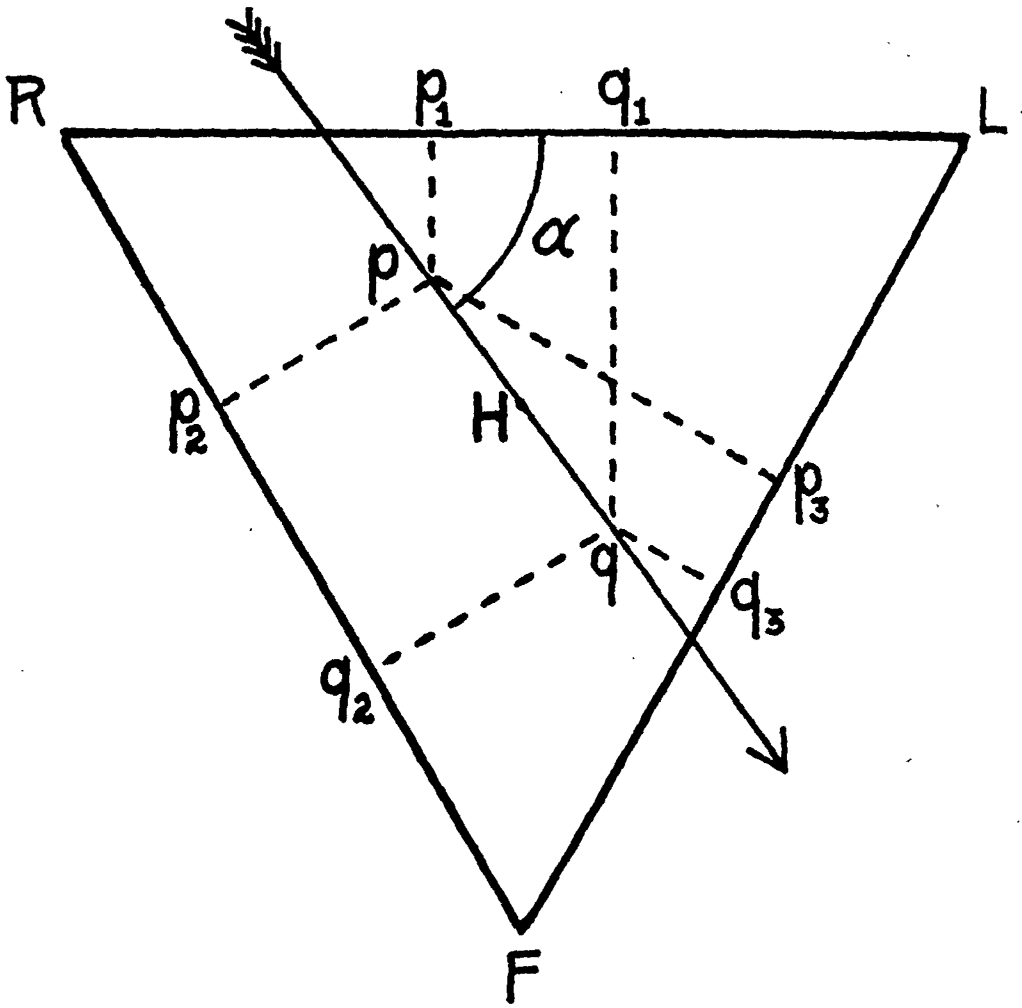
†Most of the observations upon which this article is based were made between 1915 and 1922; some of them were repeated and others were made for the first time between 1922 and 1926. The conclusions incorporated in it date from the same period. A few of the observations and some of the conclusions drawn from them have been published incidentally in papers dealing primarily with other subjects (1, p. 161; 2, p. 237 footnote; 3, p. 101 footnote). In 1926 a preliminary report calling attention to the laws which govern the flow of electric currents in solid conductors, within which a source of potential difference exists, and pointing out that these laws determine the distribution of the potential differences produced by the heart beat within the body and at its surface, was published in collaboration with Wishart and Herrmann[4]. Circumstances beyond the control of the writer have prevented the publication of the complete report until this time; it is now published in order that it may serve as an introduction to further studies based in part upon it which have been carried out recently in collaboration with MacLeod and Barker.

quently, some steps in the development of the method which appeared obvious to Einthoven have not been at all obvious to the majority of those who have made use of it.



$$pq = E$$
$$p_1q_1 = e_1 = E\cos\alpha$$
$$p_2q_2 = e_2 = E\cos(\alpha - 60)$$
$$p_3q_3 = e_3 = E\cos(120 - \alpha)$$

Fig. 1.—After Einthoven, Fahr, and de Waart[5] An equilateral triangle of homogeneous material. A potential difference is assumed to exist between two points very close together near the center of the triangle H. The arrow gives the direction of the potential difference.

In the original article the foundations of the method are described in substance as follows:

Let us assume that the equilateral triangle RLF (Fig. 1) represents a homogeneous flat plate of conducting material, and that a potential difference is produced between two points extremely close together, lying in the immediate neighborhood of its center H. Let us assume further that the line which joins the negative to the positive point has the direction of the arrow drawn through H. Upon this arrow let us lay off an arbitrary distance *pq*, and let the projections of *pq* upon the three sides of the triangle, RL, RF, and LF, be represented by e_1, e_2, and e_3 respectively. Under these conditions the potential difference between any two apices of the triangle must be proportional to the projection of *pq* upon the side of the triangle which joins them; in other words if R-L, R-F, and L-F represent the differences in potential between the corresponding apices, then R-L : R-F : L-F $= e_1 : e_2 : e_3$. Why this must be so is not explained. When the writer asked Einthoven, at the time of his last visit to America, why this explanation was omitted, he replied that it seemed obvious.

It is carefully explained that the manifest potential difference is not to be confused with the actual potential difference at the center of the triangle, of which it is but a small fraction, which varies in value with the distance between the points showing the potential difference. It is pointed out also that when this scheme is applied to the analysis of the human electrocardiogram certain assumptions are made; namely, that the heart is a material point in a homogeneous medium; that the heart is equidistant from the three points to which the electrodes are attached; and that consequently the resistances between these points and the heart are equal. It is admitted that these assumptions are not strictly in accord with the facts. The electrical resistance of the lungs differs from that of the heart and that of the chest wall. The two feet are represented in the triangle by a single point, although actually small but measurable differences of potential between them are produced by the heart beat. The results yielded by the method indicate, however, that these assumptions do not invalidate it for practical purposes.

Einthoven also points out that any potential difference generated in a direction perpendicular to the frontal plane is without influence upon the three standard leads, and that any potential difference which makes an acute angle with this plane exerts an effect proportional to the cosine of this angle.

THE EFFECT OF PLACING ONE ELECTRODE NEAR THE HEART

I first became deeply interested in Einthoven's method of analyzing the form of the electrocardiogram in 1915. I was engaged at that time in a study of atrio-ventricular rhythm. It was observed that in this condition the auricular complex was upright in lead *I* but inverted in leads *II* and *III*. The equilateral triangle seemed to offer

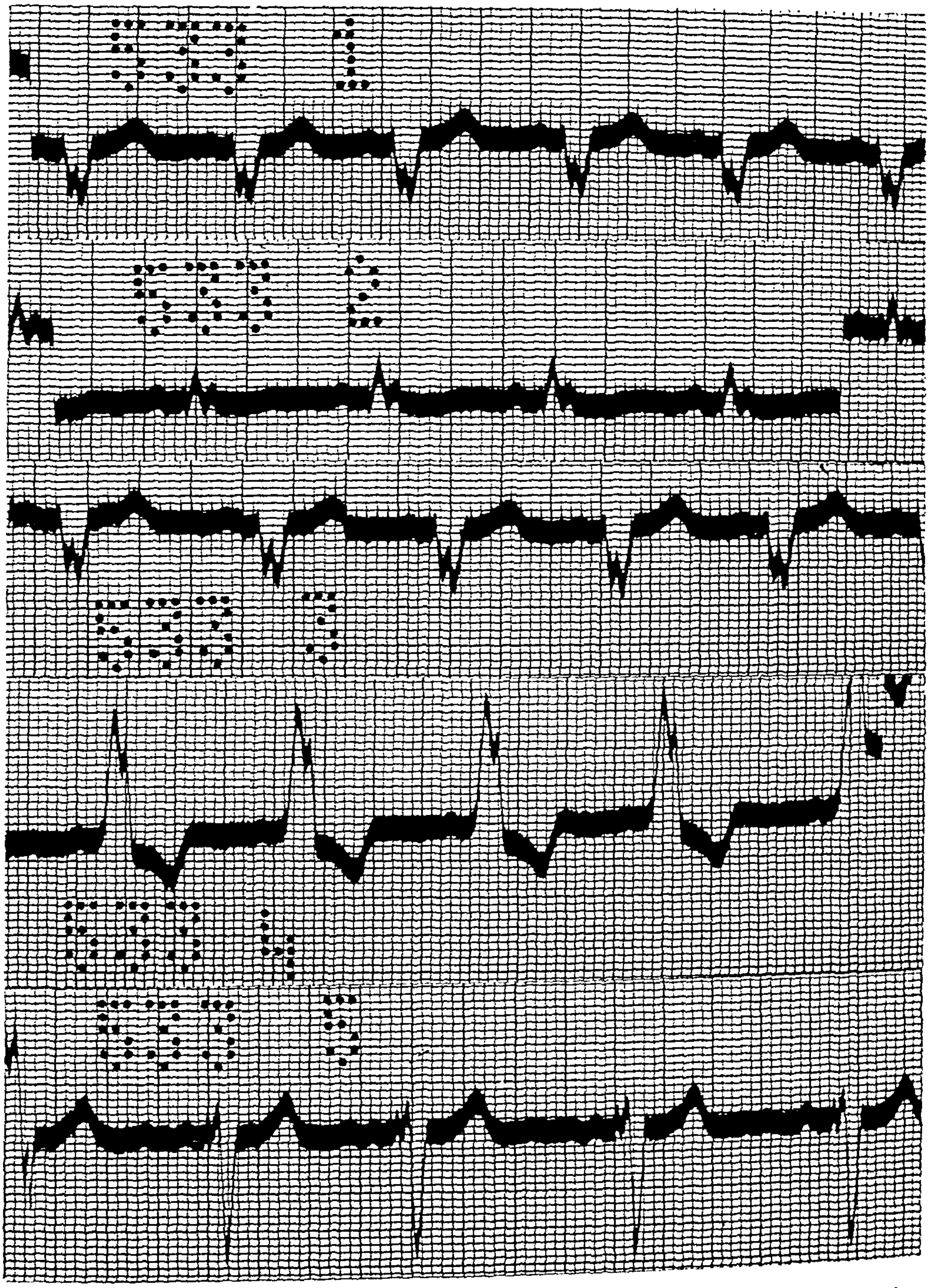


Fig. 2.—Five curves taken by means of chest leads in a case of intraventricular block.

1 cm. equals 1 millivolt, time divisions, 0.2 and 0.04 second.
533-1. *Z*-electrode in 2*sd.* i.c.s. 3.25″ to right of *midline.*
C-electrode in 2*sd.* i.c.s. 3.25″ to left of midline.
533-2. Same as 533-1 except *C*-electrode moved 2.5″ further to the left.
533-3. Same as 533-1 except *Z*-electrode moved 2.5″ further to the right.
533-4. *Z*-electrode in right axilla, *C*-electrode in left axilla.
533-5. *Z*-electrode just inside right nipple, *C*-electrode just inside left nipple.

an explanation; it indicated that the average direction of the spread of the excitation process in atrio-ventricular rhythm was upward and to the left, a conclusion apparently in harmony with the location of the atrio-ventricular node. Since, however, the triangle gave no information concerning events in the sagittal plane, an attempt was made to make the method three-dimensional by choosing four points on the body surface so arranged as to form the apices of an equilateral tetrahedron, and taking six leads corresponding to the six edges of this figure. At this time the writer was under the impression that since Einthoven appeared to treat the potential difference at the center of the triangle as if it were a mathematical vector, it could be so treated under all circumstances. I supposed that any lead from right to left must give an electrocardiogram similar to, if not identical with, that recorded in lead *I*.

When an attempt was made, however, to substitute an equilateral tetrahedron for the equilateral triangle, it was soon discovered that this was by no means the case. If two leads from right to left are taken; one from the right axilla to the left axilla and another from the right nipple to the left nipple, the chief deflections of the ventricular complex may be upright in one lead and inverted in the other. Fig. 2 illustrates this point; the subject was a patient with intraventricular block. The first curve (533-4) was taken with the *Z*-electrode (*right-hand electrode*) *in the right axilla at the level of the* nipple and the *C*-electrode (left-hand electrode) in the left axilla at the same level. Each electrode was then moved 3 in. toward the midline, so that the *Z*-electrode was just inside the right nipple and the *C*-electrode just inside the left. In the first curve the initial ventricular deflections are upright; in the second they are inverted (533-5). A second series of curves was then taken at the level of the second intercostal space. In taking the first of these (533-1) the *Z*-electrode was placed 3.25 in. to the right of the midline and the *C*-electrode the same distance to the left. The *C*-electrode was then moved 2.5 in. further to the left of the midline, the *Z*-electrode being left in place and another curve was taken (533-2). It will be seen that moving the *C*-electrode to the left changed the direction of the chief initial deflection of the ventricular complex. Moving the *Z*-electrode an equal distance to the right of the midline (533-3), the *C*-electrode being returned to its original position, had no appreciable effect. It will be noted also that the curves taken at the level of the second intercostal space are much smaller in amplitude than those taken at the nipple level, although the galvanometer was used at the same sensitivity. These observations suggest that the position of the electrode which is nearest the heart exerts the controlling influence upon the form of the resulting curve. In fact, if one electrode is placed upon the center of the precordium, the position of the second electrode, so long as it is relatively distant from the heart,

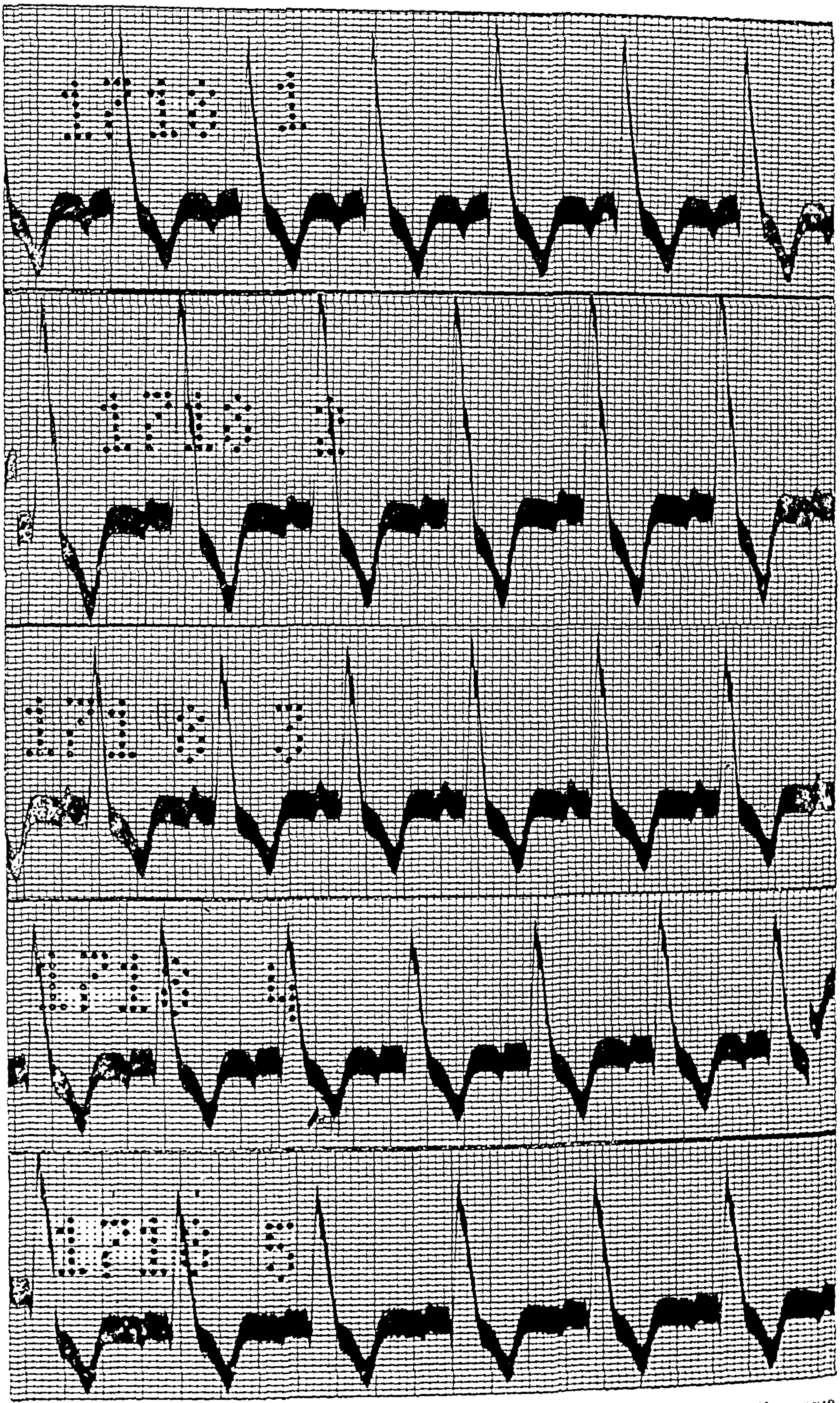


Fig. 3.—Five electrocardiograms taken by means of chest leads. From the same patient as Fig. 2. Z-electrode upon 4th costal cartilage near sternum in all instances.

1718-1. C-electrode on manubrium.
1718-2. C-electrode in left axilla.
1718-3. C-electrode on abdomen.
1718-4. C-electrode in right axilla.
1718-5. C-electrode on spine.

has little effect upon the ventricular electrocardiogram. The five curves shown in Fig. 3 were taken from the same patient as those already described. The Z-electrode was placed upon the 4th costal cartilage at its junction with the sternum; the C-electrode was placed in turn upon the manubrium (5 in. from the Z-electrode; 1718-1); in the left axilla (10 in.; 1718-2); upon the abdomen (9 in.; 1718-3); in the right axilla (8 in.; 1718-4); and upon the spine (1718-5). The ventricular complexes have the same general form in all of these courves although they differ somewhat in amplitude. It appears, therefore, that the potential differences in the immediate neighborhood of the heart are of much greater magnitude than those at a distance from it. This may be demonstrated most easily by the following experiment. Let a line be drawn from the 4th costal cartilage near the sternum to any point on the anterior aspect of the left thigh. Starting at the proximal end of this line (4th costal cartilage) divide it into equal segments five inches in length. From each of these segments take an electrocardiogram, placing the Z-electrode upon the proximal end (end toward the heart) and the C-electrode upon the distal end of the segment. A series of curves taken in this manner has been published by Wilson and Herrmann.[1] The first segment yields a curve of large amplitude; in succeeding segments the curves become rapidly smaller and from the fourth or fifth and the remaining segments no curves at all are obtained, providing the sensitivity of the galvanometer is not increased. In a similar way it may be shown that, with the galvanometer at normal sensitivity, all points upon the left leg have the same potential throughout the cardiac cycle and the same is true of all points on the left arm, and of all points on the right arm. As Einthoven pointed out points on the right leg differ only very slightly in potential from points on the left.

Einthoven's reasons for pointing out that the equilateral triangle is based upon the assumption that the three apices of the triangle are equidistant from the heart are now obvious. It is also apparent that the three standard leads have a very great advantage over any other similar system of leads that could be employed. Since all points on the right arm, for instance, have the same potential, when the galvanometer is employed at the standard sensitivity, it does not matter whether the electrode connected to this arm is placed upon the wrist, the hand, the forearm, or the upper arm; the arm acts merely as an extension of the wire attached to it; the lead is from the attachment of the arm to the trunk. The same is true of the left arm and of the left leg. If the electrodes are placed upon the trunk, however, the exact position of each electrode, particularly if it be less than 10 or 15 inches from the heart is a matter of importance. Obviously, if three points on the trunk which form the apices of an equilateral triangle are substituted for the right arm, left arm, and left leg, and

three leads corresponding to the three standard leads are employed, the resulting electrocardiograms may be analyzed by the method of the equilateral triangle, but no confidence can be placed in the results unless it can be demonstrated that the three points are equidistant from all parts of the heart, or that they are so far from the heart, that any difference between them in this respect is of no importance. The writer is of the opinion that the principles of the equilateral triangle should not be applied to any system of chest leads whatsoever, particularly if it is desired to analyze the ventricular complex. Since it is practically impossible to choose three points in the sagittal plane which form the apices of an equilateral triangle, and which, at the same time, are both distant and equidistant from the heart, it does not seem to the writer that the principles of the equilateral triangle can justifiably be employed in studying the potential differences which have an antero-posterior direction, except perhaps in the case of the auricular deflections where the error introduced by placing one electrode nearer the heart than the other appears to be less than in the case of the ventricular deflections.

Observations such as those described convinced the writer some ten years ago that he could make no progress in the analysis of the electrocardiograms taken by means of chest leads, or by placing one or both electrodes upon the surface of the exposed heart, until he understood the laws which govern the distribution of potential differences within solid conductors. A careful examination of the older electrocardiographic literature did not disclose any discussion of these laws, although it was evident that they were known to Waller as early as 1889. In a paper which appeared in that year[6] he published an outline drawing of the trunk upon which a system of iso-potential surfaces, seen in cross-section, are drawn about the heart. Waller was under the impression that the impulse spread over the ventricular muscle from apex to base in the form of a peristaltic wave; and that the muscle of the ventricles could be treated as a single unit. Consequently, he represented the iso-potential surfaces as if the apex of the heart could be treated as the negative pole or sink and the base as the positive pole or source of the potential differences produced by the ventricles. Waller used this diagram in explaining why some leads gave larger deflections than others. He did not discuss the laws upon which the diagram is based. These laws were obviously known to Einthoven also, since the equilateral triangle is founded upon them; his discussion of the assumptions upon which the application of the principles of the triangle is based shows plainly that, as might be expected from his knowledge of electrical theory, he knew and understood the factors involved thoroughly. He did not, however, discuss the laws themselves, which in so far as they apply to simple conditions can be found in almost any textbook dealing with electrical theory or with

potential function. The distribution of potential differences in a solid conductor so irregular in shape as the body cannot, of course, be determined mathematically. Nevertheless, the laws as they apply to homogeneous solids of regular shape or of infinite extent are very helpful in understanding the principles involved.

LAWS WHICH GOVERN THE DISTRIBUTION OF POTENTIAL DIFFERENCES

The potential, V, of any point in a thin homogeneous sheet of conducting material, infinite in extent, within which a potential difference

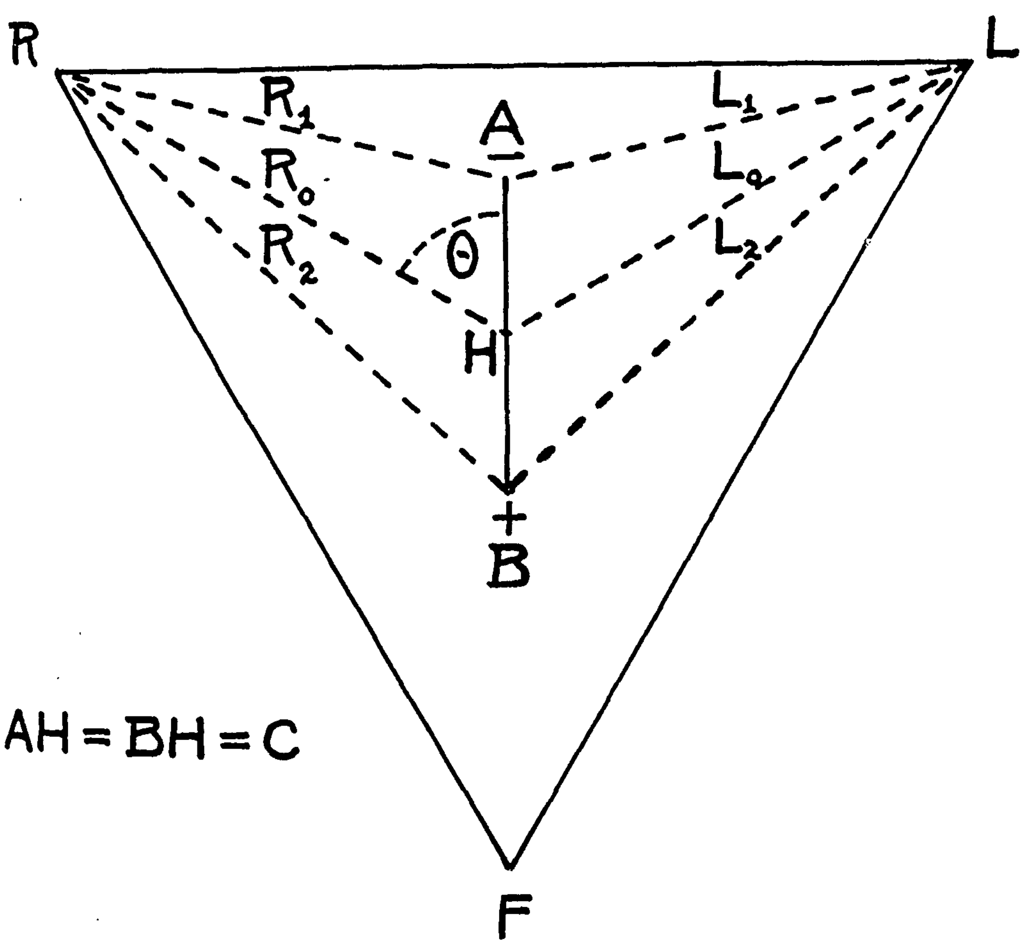


Fig. 4.—An equilateral triangle in an infinite conducting sheet or infinite conducting solid; a potential difference between A and B which are equidistant from the center H. The source of this potential difference at B (+) and the sink at A (−). C is equal to one-half the distance between sink and source. Line AB is the axis of the potential difference.

is maintained between two points close together is determined by the equation below[7];—

$$V = \frac{Q}{2\pi kd} \log_e \frac{R_1}{R_2} \qquad (1)$$

In this equation Q is the quantity of electricity flowing in unit time; k, the conductivity of the material of which the sheet is composed; d, the thickness of the sheet; and R_1 and R_2, the distances of the

point from the negative pole or sink and the positive pole or source of the potential difference respectively.

Let us construct (Fig. 4) upon this infinite sheet of conducting material an equilateral triangle RLF so placed that the sink and source of the potential difference will be near to and equidistant from the center of the triangle H. The difference in potential between two apices of the triangle, R and L, will then be determined by the following expression.

$$V_1 - V_2 = \frac{Q}{2\pi dk} \log_e \frac{R_1}{R_2} - \log_e \frac{L_1}{L_2}) \qquad (2)$$

In this expression V_1 is the potential of apex R; V_2 the potential of apex L; R_1 and R_2 the distances of R_1 and L_1 and L_2 the distances of L from sink and source respectively.

It will be seen at once that if the line joining these two apices of the triangle (RL) is perpendicular to the axis of the potential difference, that is to say to the line joining sink and source, both apices will have the same potential, for the ratio $\frac{R_1}{R_2}$ will be equal to the ratio $\frac{L_1}{L_2}$. It is also clear that the difference in potential between R and L will be maximal when the line joining them is parallel to the axis of the potential difference. It is not quite so obvious that if the sink and source are very close together the potential difference between R and L will be proportional to the cosine of the angle between the axis of the potential difference and the line RL. This may be shown as follows:

The potential V_1 of the apex R is determined by $\log_e \frac{R_1}{R_2}$. This expression may be represented by an infinite series (9); viz.,—

$$\log_e \frac{R_1}{R_2} = 2 \left[\frac{R_1 - R_2}{R_1 + R_2} + \tfrac{1}{3} \left(\frac{R_1 - R_2}{R_1 + R_2}\right)^3 \ldots\ldots \text{etc.}\right] \qquad (3)$$

$$= 2 \left[\frac{R_1^2 - R_2^2}{(R_1 + R_2)^2} + \tfrac{1}{3} \left(\frac{R_1^2 - R_2^2}{[R_1 + R_2]^2}\right)^3 \ldots\ldots \text{etc.}\right] \qquad (4)$$

Referring again to Fig. 4, it will be seen that R_1^2 is equal to $R_0^2 + C^2 - 2R_0C \cos\theta$ when R_0 is the distance of R from the center of the triangle and C is one-half the distance between sink and source. Similarly, R_2^2 equals $R_0^2 + C^2 + 2R_0C \cos\theta$.

If we substitute these values of R_1^2 and R_2^2 in equation (4) we get

$$\log_e \frac{R_1}{R_2} = 2 \left[\frac{-4\, R_0C \cos\theta}{(R_1 + R_2)^2} + \tfrac{1}{3} \left(\frac{-4\, R_0C \cos\theta}{(R_1 + R_2)^2}\right)^3 \ldots\ldots \text{etc.}\right] \qquad (5)$$

If sink and source are extremely close together R_1 and R_2 will become practically equal to R_0 and this expression will become

$$\log_e \frac{R_1}{R_2} = 2\left[\frac{-C\cos\theta}{R_0} + \tfrac{1}{3}\left(\frac{-C\cos\theta}{R_0}\right)^3 \ldots\ldots \text{etc.}\right] \qquad (6)$$

This series is rapidly convergent and since R_0 is very large we may neglect all terms except the first. In that case

$$\log_e \frac{R_1}{R_2} = \frac{-2\,C\cos\theta}{R_0}. \quad \text{Hence } V_1 = \frac{Q}{2\pi dk}\left(\frac{-2C\cos\theta}{R_0}\right) \qquad (7)$$

Since $\angle RHL$ equals $120°$ and R_0 equals L_0, it may be shown in the same way that, if V_2 is the potential of L

$$V_2 = \frac{Q}{2\pi dk}\left[\frac{-2\,C\cos(120° - \theta)}{R_0}\right] \qquad (8)$$

$$\text{Consequently, } V_1 - V_2 = \frac{Q}{2\pi dk}\left[\frac{-2\,C}{R_0}\right]\left[\cos\theta - \cos(120° - \theta)\right] \qquad (9)$$

But θ may be expressed in terms of α, the angle between the axis of the potential difference and the line RL for as may be seen from Fig. 4, $\theta = \alpha - 30°$. Therefore,

$$V_1 - V_2 = \frac{Q}{2\pi dk}\left[\frac{-2\,C}{R_0}\right]\left[\cos(\alpha - 30°) - \cos(150° - \alpha)\right] \qquad (10)$$

$$V_1 - V_2 = \frac{Q}{2\pi dk}\left[\frac{-2\,C}{R_0}\right]\left[\sqrt{3}\cos\alpha\right] \qquad (11)$$

Q.E.D.

The expression for the potential of any point in a homogeneous conductor of which all the dimensions are infinite is even more simple[8] than that which holds for an infinite thin sheet. It is

$$V = K\left(\frac{1}{R_2} - \frac{1}{R_1}\right) \qquad (12)$$

In this expression K is a constant depending upon the conductivity of the medium and the quantity of electricity flowing in unit time, and R_1 and R_2 are the distances of the point from the sink and source respectively.

In this case also it may be shown that if an equilateral triangle is so placed in the medium that its apices lie in the same plane as the sink and source, and the sink and source are very close together and

equidistant from the center of the triangle, the difference in potential between any two apices of the triangle will be proportional to the cosine of the angle between the line joining them and the axis of the potential difference at the center. For, referring again to Fig. 4,

$$V_1 = K\left(\frac{1}{R_2} - \frac{1}{R_1}\right) = K\left(\frac{R_1 - R_2}{R_1R_2}\right) = K\left[\frac{R_1^2 - R_2^2}{R_1R_2(R_1 + R_2)}\right] \quad (13)$$

If in this expression we substitute for R_1^2 and R_2^2 their values in terms of R, C and θ we get,

$$V_1 = K\left[\frac{-4\,R_0C\cos\theta}{R_1R_2(R_1 + R_2)}\right] \quad (14)$$

When the sink and source are extremely close together so that R_1 and R_2 become practically equal to R_0 this expression becomes

$$V_1 = K\left[\frac{-2\,C\cos\theta}{R_0^2}\right] \quad (15)$$

The remainder of the proof is the same as in the case of an infinite sheet.

In case the sink and source do not lie in the same plane as the triangle so that the line joining them makes an angle with this plane, the effect of the potential difference between them in this plane will be proportional to the cosine of this angle.

It will be observed that the potential difference between any two apices of the triangle (Fig. 4) varies directly with C and consequently it will become greater as the sink and source are further apart. Furthermore since the potential difference varies inversely with R_0 or with R_0^2 according to whether we are dealing with a thin sheet or an infinite solid, the difference in potential will become smaller as R_0 increases. Einthoven's reasons for stating that the manifest potential difference is only a small fraction of the actual potential difference, and that this fraction varies with the distance between the points showing the potential difference, are now obvious.

ILLUSTRATIVE EXPERIMENTS

In order to illustrate the effect of some of the factors involved the writer, in 1922, performed some experiments upon a model. A large shallow pan upon the bottom of which a large equilateral triangle had been drawn was partially filled with weak copper sulphate solution. The three lead wires of the galvanometer were attached to electrodes placed at the apices of the triangle. At the center of the triangle and equidistant from it two other electrodes were placed and these were

connected to the terminals of the secondary coil of an inductorium. The primary circuit of this inductorium was opened and closed rhythmically by a device which short-circuited the secondary coil at the time when the primary circuit was closed so that only break shocks were delivered to the electrodes at the center of the triangle. The effect of these shocks upon the differences in potential between the apices of the triangle was recorded with the string galvanometer. A summary of these experiments is given in Table I.

It will be seen that the deflections in the three leads are proportional, or nearly proportional, to the cosine of the angle between the

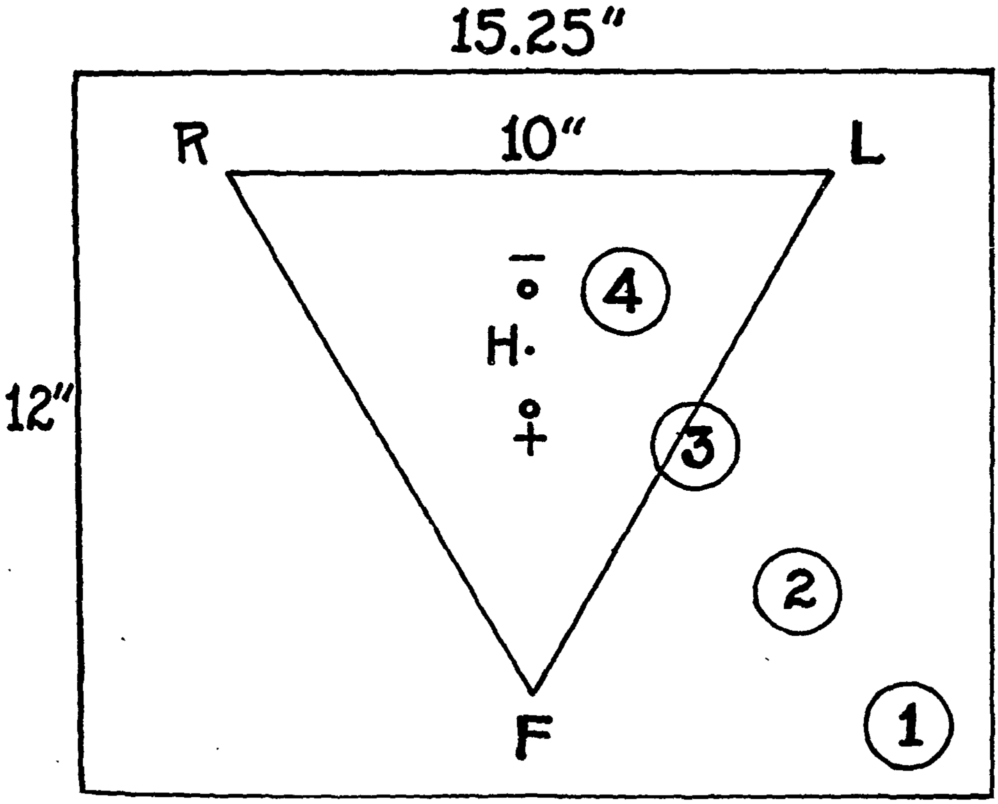


Fig. 5.—An equilateral triangle drawn upon the bottom of a large flat dish containing a weak solution of copper sulphate. The three usual lead wires were attached to the apices of *the triangle*. *Rhythmic induction shocks were delivered to the* electrodes near the center *H*. The circles show the positions of a coil of wire in an experiment described in the text.

line of lead and the axis of the potential difference so long as the sink and source are equidistant from the center of the triangle. If, however, the sink and source are moved to the right or left so that the midpoint of the line which joins them is no longer equidistant from the apices of the triangle this is no longer the case, the direction of the deflection in any lead being then largely determined by the relative distance from the sink and source of the apex which is nearest this point. It will also be observed that in accordance with the laws which describe the flow of currents in solid conductors the manifest potential difference increases with the distance between sink and source.

TABLE I

NO. OF OBSERVATIONS	LENGTH OF SIDE OF TRIANGLE	C**	α††	LI	LII	LIII
1	9.6″	0.65″	30°	14	15	1
2	9.6″	1.00″	30°	17	19	2
3	9.6″	1.50″	30°	26	27.5	1
4	9.6″	1.25″	0°	17	8	–9
5	10.5″	0.68″	90°	–2	7	11
6*	10.5″	0.68″	90°	–5	6	10
7†	10.5″	0.68″	90°	1	7	7
8‡	10.5″	0.68″	90°	4.5	8	3.5

*Both electrodes moved 1.25″ to right (i.e. toward side RF in Fig. 4).
†Both electrodes moved 1.25″ to left (toward side LF in Fig. 4).
‡Both electrodes moved 2.5″ to right and 1.5″ upward.
**C is one half the distance between sink and source.
††α is the angle between the line joining sink and source and line RL (Fig. 4).

In order to determine the effect of changing the resistance between two apices of the triangle upon the difference in potential between them a coil of copper wire was placed in the copper sulphate solution. The various positions of the coil are shown in Fig. 5. The corresponding deflections in lead *III* were as follows; coil out, 18; coil at 1, 16; coil at 2, 13; coil at 3, 9; coil at 4, 6 mm. It will be seen, therefore, that as the coil was moved toward the source of potential difference the magnitude of the deflection in lead *III* rapidly decreased until it reached one-third its value with the coil out.

APPLICATIONS TO DIRECT AND SEMI-DIRECT LEADS

We may now discuss briefly the application of the principles which govern the distribution of potential differences in solid conductors to the analysis of electrocardiograms obtained by direct leads or by indirect leads in which one electrode is placed nearer the heart than the other.

As Lewis[10] has pointed out, the heart muscle cannot be regarded, from the electrocardiographic standpoint, as a single unit; it is obviously made up of a large number of individual units, each of which produces its own electrical effects. Consequently, many sinks and sources must exist within the heart throughout the period of its electrical activity. When the electrodes are placed upon points distant from the heart, all of the muscle units will be equal or practically equal, with respect to their distance from the electrodes and all parts of the heart will have an equal opportunity to exert their influence upon the form of the electrocardiogram. When, on the other hand, one electrode is placed much nearer to the heart than the other, this is no longer the case. The potential variations of the electrode which is placed close to the heart will not only be very much greater than those of the distant electrode, but they will represent the activity of various portions of the heart unequally. Those portions of the heart which are nearest to the electrode which is near by must exert a very much greater effect in proportion to the potential differences which they

produce than those parts of the heart which are further away. Lewis[10] and his associates have shown that when one or both electrodes are placed directly upon the exposed heart, two types of effects can be distinguished; intrinsic effects which are the result of the activity of the muscle immediately beneath the electrode or electrodes placed upon the heart muscle, and extrinsic effects produced by the activity of muscle that is at a distance. It is obvious, however, that an electrode which is placed upon the heart bears no special relation to the subjacent muscle except that of nearness, and that there can be no fundamental difference between placing an electrode actually upon the muscle and placing an electrode close to it, provided of course that in the second case the electrode is not separated from the muscle by a non-conducting substance.

When one electrode is placed upon the precordium and the other at a point relatively distant from the heart, the precordial electrode is much nearer the anterior wall of the heart than the posterior; consequently the electrical activity of the anterior wall of the heart has a much greater effect upon the form of the curve than the electrical activity of the posterior wall, just as the subjacent muscle exerts a more pronounced effect than the more distant muscle in the case of direct leads. Leads in which one electrode is placed close to the heart are therefore semi-direct leads. It is not surprising that the curves obtained from such leads are in many respects similar to those obtained by placing one electrode upon the exposed heart. In both cases the position of the second electrode, so long as it is placed upon a point distant from the heart, has comparatively little effect upon the form of the curve recorded. When one electrode is placed upon the ventricular surface and the other upon a distant point, the arm or leg for instance, deflections are obtained which have a value of 40 to 80 millivolts, a value approximately 20 times that of the tallest deflections that occur in the standard leads. Since the arm and leg do not show a difference of potential exceeding three or four millivolts at any time during the cardiac cycle, which extremity is used as the distant point is relatively immaterial. Consequently, when one electrode is placed upon the heart and the other upon one of the extremities the resulting curve is, for all practical purposes, a record of the variations in potential of the electrode placed upon the heart. The potential variations of a point upon the precordium are very much smaller than the potential variations of a point upon the heart; they are still five to ten times as great as the potential variations which occur at points upon the extremities.

Let us now examine the curves which are obtained by placing one or both electrodes upon the auricular muscle where the course of the excitation wave is a relatively simple one. Lewis[10] and his collaborators found that if the *Z*-electrode was placed upon the sinus node and

the C-electrode a short distance from it the first deflection of the resulting electrogram began with a sharp upright deflection, the intrinsic deflection due to activation of the muscle beneath the Z-electrode. If now the Z-electrode was placed a short distance from the node and the C-electrode still further away the electrogram still showed a sharp upstroke signaling the arrival of the excitation process at the Z-electrode, but in this case the intrinsic deflection was preceded by a small deflection downward due to muscle activity at a distance; an extrinsic effect. Obviously, however, this extrinsic effect must be the result of the activation of the muscle immediately about the sinus node for no other muscle is active at the time when it occurs. All of the potential differences which exist under these circumstances must be closer to the Z-electrode than to the C-electrode. Since the extrinsic deflection indicates relative positivity of the Z-electrode this electrode must lie nearer to the positive pole or poles or further from the negative pole or poles than the C-electrode. Since, however, all of the active muscle is nearer the Z-electrode than the C-electrode the second alternative is impossible. Consequently it must be concluded that the positive pole lies between the Z-electrode and the active muscle, which is known to show relative negativity. The excitation process must therefore consist in a negative and a positive pole lying relatively close together. Were it not so it would be difficult or impossible to distinguish between intrinsic and extrinsic effects. If, for instance, the excitation process be regarded as a wave of negativity, the whole of the unexcited muscle being regarded as the positive pole, the Z-electrode should become more and more negative as the excitation wave approached it; it could never become relatively positive until the wave of negativity had passed the midpoint between the two electrodes, so that the negative pole of the potential difference was closer to the C-electrode than to the Z-electrode. Under these circumstances there could be no sharp upstroke marking the arrival of the excitation process at the electrode nearest the sinus node, except in the case where this electrode was placed upon the nodal region.

THE CONDUCTIVITY OF THE BODY TISSUES

According to equation (2) the potential difference between apices R and L of the equilateral triangle (Fig. 4) varies inversely with the electrical conductivity of the material within which the source of potential difference exists. We may predict, therefore, that any increase in the conductivity of the body tissues, particularly of those tissues which lie in close proximity to the heart, will decrease the amplitude of the electrocardiographic deflections.

It is well known that in many cases of advanced cardiac disease electrocardiograms of very small amplitude occur. It is generally believed that such curves are the result of a decrease in magnitude of

the potential differences produced by the diseased heart muscle. Admitting that in many, if not in most instances, this is the most reasonable explanation of curves of small amplitude, we may point out that an increase in the conductivity of the body tissues, particularly of those tissues which lie close to the heart, may produce the same result. The lungs because of the large amount of air which they contain must, as Einthoven pointed out, have a somewhat lower electrical conductivity than the chest wall or the heart. The question arises, therefore, as to whether edema of the lungs, pericardial effusion, pleural effusion, hydrothorax, ascites, or massive edema of all the body tissues may not decrease the amplitude of the electrocardiographic deflections.

With this in mind I examined a small group of unselected cases in which electrocardiograms of small amplitude had been recorded. In these cases all of the electrocardiographic deflections were small in all leads; the QRS deflection of largest amplitude did not exceed 0.6 millivolt in value. Of the 24 cases studied, 14 showed advanced cardiac failure with pronounced edema, often associated with hydrothorax or ascites. There were 2 cases of cardiac failure with slight edema and 2 of cardiac failure without evident edema at the time of the examination. There was one case of Hodgkin's disease with massive pleural effusion, and one case of pulmonary tuberculosis and aortic regurgitation with ascites, but without signs of cardiac failure. The clinical diagnoses in the remaining four cases were as follows; arteriosclerosis without cardiac failure, Addison's disease, diabetes mellitus, and pernicious anemia. None of these last patients had cardiac failure, edema, ascites, or other accumulations of fluid at the time of the examination, although the patient with pernicious anemia gave a history of very recent pronounced edema.

In those cases in which cardiac failure and edema were both present, it is, of course, impossible to say whether the condition of the heart muscle or the presence of edema was responsible for the small amplitude of the electrocardiographic deflections. There seems, however, to be a tendency for small curves to occur in patients with edema, ascites, or pleural effusion who have no cardiac failure. In these it is possible that a change in the conductivity of the body tissues is the cause of the small curves. In still other cases the small amplitude of the electrocardiograms is very probably more or less accidental, and is due to the fact that the potential differences produced by one part of the heart are almost exactly neutralized by those produced in other parts, so that the resultant potential difference is very small. This is undoubtedly the explanation in those cases where only part of the electrocardiographic deflections are small; that is to say when only the ventricular or only the auricular complex is affected. Changes in the conductivity of the body tissues must affect the amplitude of all of the

deflections equally, and the same is probably true to a lesser extent of changes in the condition of the heart muscle.

SUMMARY

The foundations of Einthoven's equilateral triangle are discussed and it is pointed out that it is based upon certain assumptions to which Einthoven called particular attention, but the importance of which has not always been borne in mind.

The laws which govern the distribution of potential in solid conductors are described, and it is pointed out that a knowledge of these laws is essential to the analysis of those electrocardiograms obtained by chest leads in which one electrode is placed nearer the heart than the other, and in the analysis of the curves obtained by direct leads.

Leads in which one electrode is placed upon the precordium and the other at a distant point are semi-direct leads. In such leads the electrical effects of that part of the heart wall nearest the precordial electrode are exaggerated.

The excitation wave cannot be regarded as a wave of negativity, since the positive pole of the potential difference which it produces is close to the negative pole. It is this fact which makes it possible to distinguish between intrinsic and extrinsic effects in direct leads.

An increase in the conductivity of the body tissues, particularly of those which are close to the heart must decrease the amplitude of the electrocardiographic deflections. It is suggested that in certain instances accumulations of fluid near the heart or massive edema may act in this way.

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PARTIAL BUNDLE-BRANCH BLOCK

A CASE OF THREE-TO-ONE AND FOUR-TO-ONE BLOCK*

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A RECORD was obtained in the electrocardiographic laboratory which presented such interesting features that its report has seemed warranted. Furthermore, a very extensive search into the literature has failed to reveal a similar electrocardiogram. It is the belief of the writer that it is the first of its kind on record. It was interpreted as partial bundle-branch block in which there was a three-to-one and four-to-one block of the right branch of the bundle of His.

The patient presented herself to the electrocardiographic department on the afternoon of January 8, 1930, at the request of the Thyroid Clinic of the Jewish Hospital. Only a short strip was taken—Fig. 1 representing its entire length. Because of its interest other records were taken that evening, at the same time certain tests being made. As a result of the ergotamine tartrate (gynergen) which she received she began to vomit, felt weak and had to be admitted to the hospital on the service of Dr. Joseph Rosenthal. The following history was obtained and physical findings noted:

G. G., aged forty years, born in Russia was admitted the evening of January 8, 1930 with a story of vomiting, palpitation and dyspnea for the past six weeks. She was short of breath and complained of marked palpitation and progressive weakness. She had lost 25 pounds in six weeks. She was also troubled by a choking sensation and difficulty in swallowing.

On physical examination there was presented a very thin short slightly built female adult who looked much older than her given age. There was a moderately fine tremor of the tongue and an acetone odor to her breath. Pigmentation of the skin of the face and neck was noted. The isthmus of the thyroid gland was palpable. Marked tachycardia was present on admission and the limits of heart dulness were increased. There was a soft systolic murmur present at the apex. These latter findings disappeared. There was impairment of resonance at the right apex and an occasional râle, crepitant in nature, was present after coughing. She had never received digitalis before admission.

Laboratory Data.—The blood study showed a secondary anemia; 4,000,000 erythrocytes and 45 per cent hemoglobin. The blood chemistry was normal and the Wassermann reaction was negative. The urine showed a faint trace of albumin, no sugar and a marked acetone reaction. The sputum examinations were all negative. The basal metabolism showed a plus 30 per cent rate. The x-ray plate of the lungs showed a bilateral hilum infiltration. The blood pressure was 140/70 to 130/50 mm. Hg. The teleroentgenogram of the heart read "Cardiac shadow is within normal limits of size, shape and position." The diagnosis therefor was acute hyperthyroidism with myocardial involvement.

*From the Department of Cardiology, Jewish Hospital of Brooklyn, N. Y.

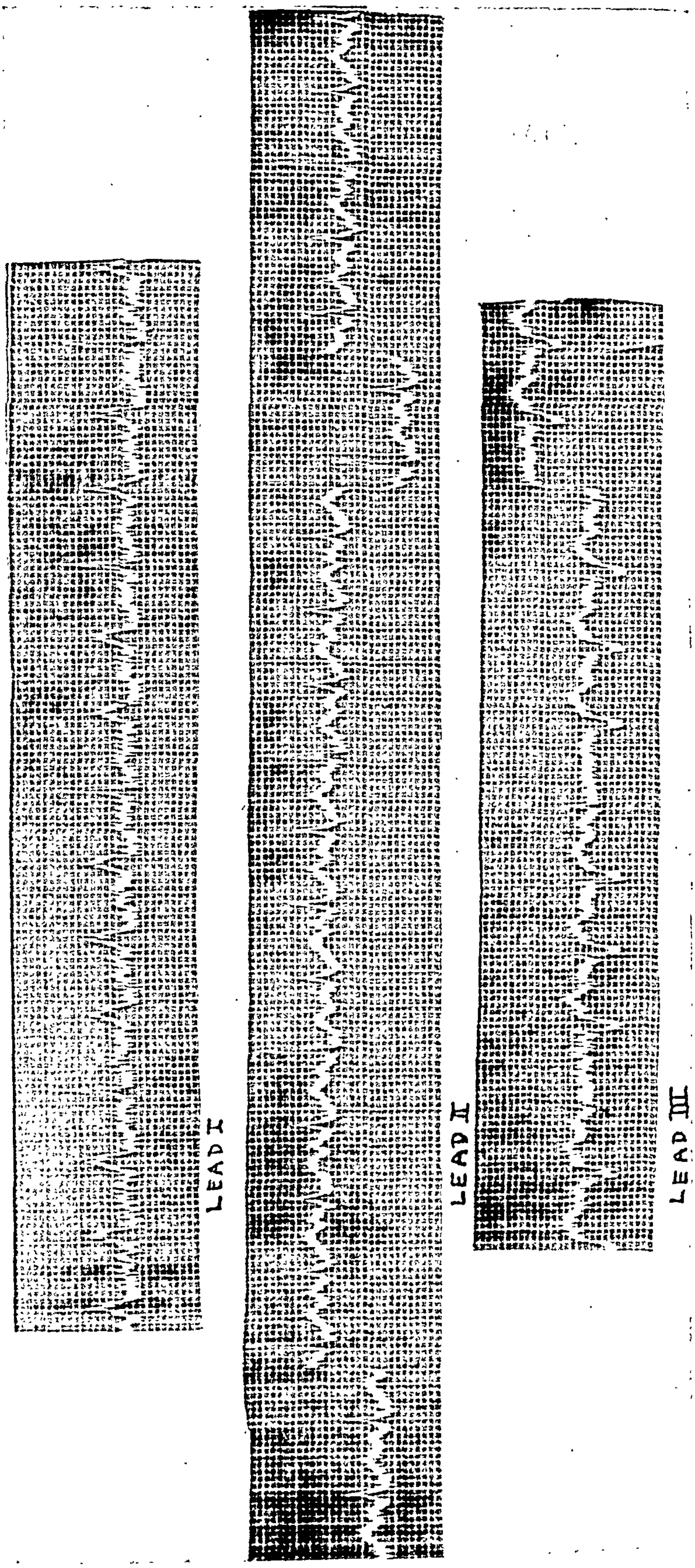

Fig. 1.

DISCUSSION OF THE ELECTROCARDIOGRAMS

The first electrocardiogram was taken on the afternoon of January 8, 1930. (Fig. 1.)

The examination of lead one shows the first three complexes are wide, slurred and notched with an oppositely directed T-wave coming off directly from the downlimb of the R. The first two complexes are distorted somewhat due to irregularity in the running of the camera. The QRS measures 0.12 second. The fourth complex is normal in contour and the T is directed upward. The QRS of this complex measures 0.06 second. This latter complex is followed by three complexes similar to the first three, and the eighth complex is again of normal configuration. The ninth and tenth complexes are wide and broad like the first three and are followed by another normal complex. Again two more abnormal complexes, which are followed by another normal complex. The P cannot be definitely determined in this lead. Because of the somatic tremor (the patient had acute hyperthyroidism), measurements may not be exactly accurate although they were made on many different occasions until absolute correspondence was obtained. These measurements for lead one are as follows: the ventricular rate is 140.8 per minute; the P-R interval could not be measured in this lead; the QRS of the abnormal complexes measured 0.12 second and that of the normal complex 0.06 second. R-R intervals are as follows:

R-R	1.	.410?	R-R	8.	.415
	2.	.450?		9.	.425
	3.	.440		10.	.425
	4.	.410		11.	.410
	5.	.440		12.	.425
	6.	.425		13.	.435
	7.	.435		14.	.425

In lead two, the first two complexes are short and widened, so that the QRS of each of these complexes measures 0.12 second. The third complex is normal. The R is high and measures 0.06 second. This is followed by three abnormal complexes like the first two and then again a normal complex. The second normal complex is followed by three abnormal complexes after which comes the third normal complex. The fourth and fifth normal complexes are also preceded by three abnormal complexes. The P in this lead can be measured fairly accurately. The ventricular rate is 140.3 per minute. The P-R and R-R intervals are as follows:

P-R	1.	.125	R-R	1.	.430
	2.	.120		2.	.435
	3.	.140		3.	.420
	4.	.140		4.	.425
	5.	.120		5.	.435

P-R		R-R	
6.	.130	6.	.430
7.	.130	7.	.415
8.	.120	8.	.425
9.	.115	9.	.430
10.	.125	10.	.440
11.	.125	11.	.410
12.	?	12.	.440
13.	.120	13.	.425
14.	.120	14.	.435
15.	.120	15.	.410
16.	.125	16.	.435
17.	.130	17.	.435
18.	.125	18.	.430
19.	.125	19.	.415
20.	?	20.	.420

The QRST of the abnormal complexes measures 0.320 second, and that of the normal complexes 0.285 second, a difference of 0.035 second. The third lead shows the first complex with a deep S, notched at its apex, the entire QRS widened and the T oppositely directed, coming off directly from the upstroke of the S. The next R is low but of normal configuration and narrow so that the QRS measures 0.05 second. Its T is low and entirely different from the previous T. This is followed by three complexes like the first one, after which a complex like the second or the normal occurs. This second normal is followed by three abnormal complexes and then a third normal complex. The ventricular rate is 135.6 per minute. The P-R and R-R intervals measure as follows:

P-R		R-R	
1.	.140	1.	.440
2.	.145	2.	.425
3.	.135	3.	.430
4.	.135	4.	.440
5.	.140	5.	.440
6.	.140	6.	.430
7.	.130	7.	.435
8.	.145	8.	.430
9.	.145	9.	.440
10.	.145	10.	.430
11.	.130	11.	.445
12.	.140		

How is this to be interpreted? The first three complexes of lead one and all those similar in that lead, the first two complexes in lead two and all those similar in lead two, and the first complex in lead three and all those similar in lead three indicate that there is a disturbance of conduction in the right branch of the bundle of His. These complexes are constantly present and are the only ones present in every electrocardiogram taken on this patient after January 8, 1930. These complexes are widened much beyond 0.1 second, they are diphasic in leads one and three and also in lead two in many of the subsequent records. The most important characteristics of bundle-branch block are the widening of the complex beyond 0.1 second and an oppositely directed T, constituting a diphasic complex. The height is influenced by

many factors.[35] The complex would have been higher and broader but for the fact that the heart of the patient was small. The left ventricle was not enlarged. This is extremely important for the size and width of the complexes (Wenckebach & Winterberg[37]). The x-ray examination of the heart and the clinical findings all reveal the heart of normal size and shape. It is known that in typical bundle-branch block produced on the dog that the complexes may be lower than those before the cut was made.[35] How are we to regard complexes four, eight, eleven and fourteen of lead one, complexes three, seven, eleven, fifteen and nineteen of lead two and complexes two, six and ten of lead three? Leads two and three show that all complexes, the abnormal and the normal are preceded by a P-wave. In lead one this also is so, but it is not sufficiently clear. The assumption is that all the complexes are therefor of supraventricular origin. I believe that these complexes are normal in appearance because there is the algebraic summation of a dextrocardiogram and a levocardiogram, for I believe that the impulse traveled down from the A-V node and without being blocked this time descended both branches and activated both ventricles simultaneously. The abnormal complex is that of a levocardiogram due to temporary block of the right branch of the bundle of His. This block lasts either 1.71 to 1.72 seconds or occasionally 1.255 seconds requiring almost all the time with two exceptions, the former figures for recovery.

There is only one possibility which suggests itself in view of the work of Wilson and Herrmann[36] but if directed against my interpretation can easily be answered. The possibility may exist that an extrasystole may occur just below the point of blockage in the right branch, come at the exact time to complete the activation of the right ventricle at exactly the same time as the activation of the left ventricle from the supraventricular impulse and produce the normal cardiogram. If the figures of the R-R interval are looked into, it will be seen that the R-R interval preceding the normal complex is always longer and by a good deal over that of the R-R interval following the normal complex. If this were an extrasystole, the opposite should be true. As a matter of fact, in the curves shown by Wilson and Herrmann[36] measurement shows that the pause is almost every time longer after the extrasystole is provoked than the period before and never shorter. A point might be raised that the R-R interval is shorter after the normal complex than before the normal complex because the R-R interval before includes the widened QRS of the complex that precedes the normal one. The following figures chosen at random but illustrating what occurs in all of them is shown. The interval R-R before complex seven of lead two is 0.430 second. The following R-R is 0.415 second. Now if 0.06 second were added it would make it 0.421 second the 0.06 second being the difference between the normal and the ab-

normal complex. Nor is this changed by the P-R interval. The P-R interval of the normal complex is 0.130 second and of the next complex 0.120 second, so that in this case 0.01 second might also be added. All in all the R-R interval after the normal beat is still shorter than the R-R interval before the normal beat. As a matter of fact, every measurement throughout the record shows this same state of affairs, that is, a much shorter time of the R-R interval after the normal complex than the previous R-R interval. Not only that but the figure of the R-R interval after each normal complex is below the general average. I believe that it is due to the influence of the extracardiac nerves and it may be the factor which caused conduction to improve in the right branch of the bundle of His and transmit the supraventricular impulse.

The second point against the conception of an extrasystole coming at such a time so as to form a normal complex is the P-R interval. In no place where it can be measured accurately does the normal R come before the average time. There is no shortening of the P-R interval indicative of an extrasystole arising late in diastole.

If these are extrasystoles arising in the right branch in the bundle of His below the block, we might expect, though not always, a definite coupling with the previous beat. In lead one the R-R interval **3** is 0.440 second, R-R **7** is 0.435 second, R-R **10** is 0.425 second, R-R **13** 0.435 second. The difference is 0.15 second. In lead two the difference is 0.10 second and in lead three no variation. If the coupling is constant, differences as much as 0.15 would have produced enormous differences in the summation in the dextrocardiogram and levocardiogram. Wilson and Herrmann[36] showed that retardation of as little as 0.005 second of either the levocardiogram or the dextrocardiogram produced very definite differences in the complexes. There is no need to go into this any further. All the normal complexes are similar in each of the leads.

Another fact is that these normal complexes are too regular and constant in their occurrence and configuration.

I do not believe one can seriously doubt that they are normally conducted impulses from a supraventricular origin in both branches of the bundle of His. Fig. 2 indicates what I believe has taken place. We thus have a case of three-to-one and four-to-one right bundle-branch block comparable to that of auriculo-ventricular block of the same nature. The closest record to mine is one reported by Hewlett.[10] He shows, in his diagrams a levocardiogram and then a normal complex, or two levocardiograms and then a normal complex. But in his case the cycle before the extrasystole is short and that after the extrasystole longer than any R-R interval, making a compensatory pause. Furthermore there is a shortened P-R interval. There is no doubt of

his case being extrasystolic in nature, but my record shows nothing like this. In Stenström's last case he showed a five-to-three block in one part of his record.[31]

Such a diagnosis was suspected when the record was first seen and with this in mind the patient was recalled that evening and another tracing taken (Fig. 3). As can be seen the complexes were all of those of right bundle-branch block. The ventricular rate in leads one and two was 117.6 per minute and toward the end of a lead three 127.6 per minute. It would be natural to expect that with the lower rate conduction would improve but it did not. An attempt was made to alter the chronotropic, dromotropic and bathmotropic influences. This

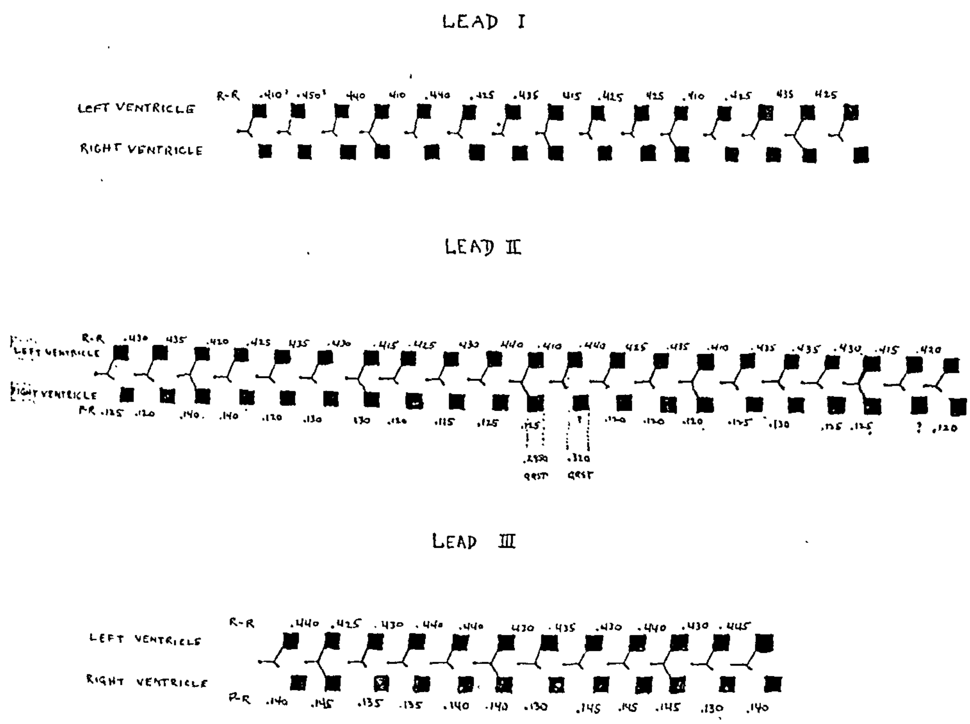

Fig. 2.—The diagram is not meant to show P-R conduction. It only illustrates the conduction from the auriculo-ventricular node down the common branch and into the right and left branches. The P-R intervals mentioned numerically under each lead are for the purpose of quick orientation.

was done for the entire next month but without succeeding in obtaining another record like that of Fig. 1. That night she was exercised, vagal pressure aplied and gynergen given. Conduction in the right branch of the bundle of His could not be improved (Fig. 4). Because the response was not as definite and perhaps not carried out under the best possible conditions, comment will not be made on this record.

On January 17, 1930, the electrocardiogram showed a typical right bundle-branch block with a ventricular rate of 101.7 per minute (Fig. 5). On that day 0.5 c.c. of adrenalin was given subcutaneously. The record shows that the rate went up to 122.4 per minute and later returned to 90.7 per minute with a short P-R interval and higher QRS

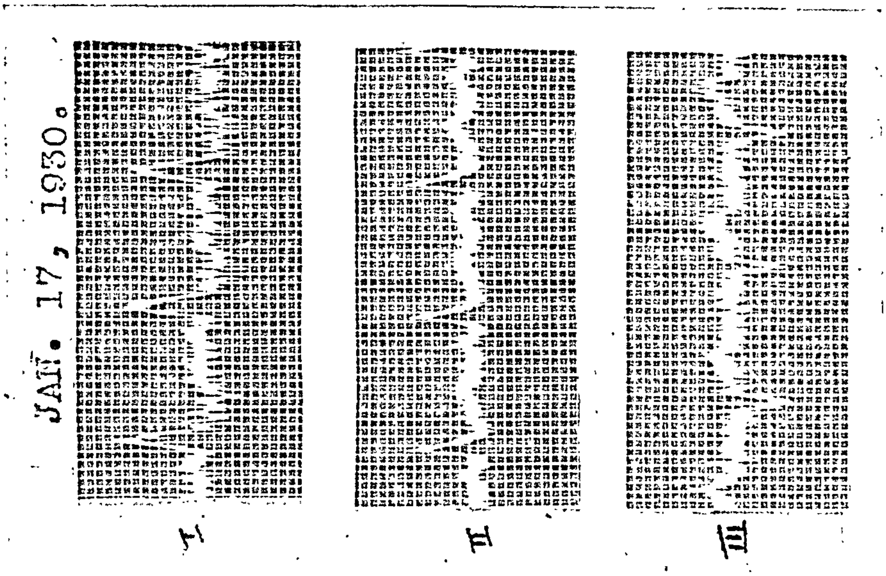

Fig. 5.

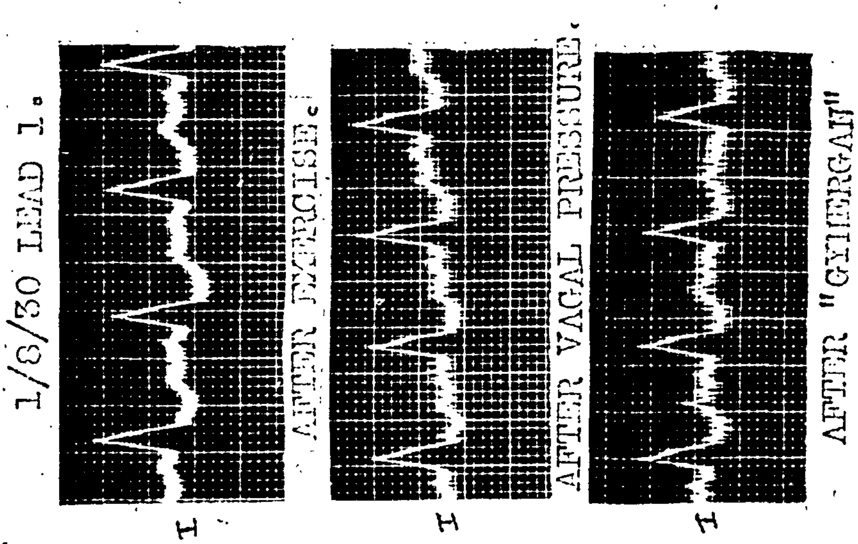

Fig. 4.

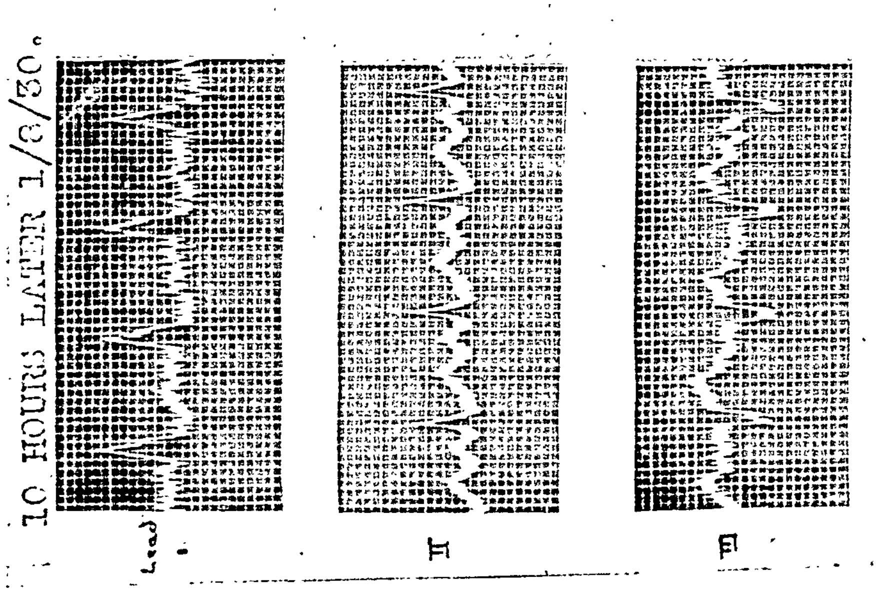

Fig. 3.

complexes (Fig. 6). On January 21, 1930, another electrocardiogram was taken which showed a ventricular rate of 101.4 per minute. Its other characteristics were as before. On the same day after Fig. 7 was taken, various tests were tried, the responses to which are shown in Fig. 8. These responses are characteristic of all the reactions which were obtained in the hospital. On vagal pressure there was practically no slowing. After exercise the rate went up to 171.4 per minute. This represents only part of the record. In view of the fact that the rate of 140.3 per minute seemed best for the production of a rhythm like Fig. 1, continuous strips after exercise were taken repeatedly so that when the rate returned to the above figures the rhythm such as that of Fig. 1 might return. However it never did.

On January 22, 1930, 0.5 c.c. of gynergen was given subcutaneously with the usual typical result. The rate before injection was 117.6 per minute and rose to 136.3 per minute (Fig. 9). Fig. 10, taken on January 28, 1930, shows a typical right bundle-branch block. Fig. 11 was taken January 30, 1930. Notice that the ventricular rate is 142.6 per minute, almost the same rate as of Fig. 1, and yet an extremely long strip did not reveal any improvement in conduction.

All these records are reproduced for the purpose of showing her subsequent course and the inability to improve conduction by all the methods tried. It is not our purpose in this paper to discuss the pharmacological aspects of her response to the various drugs.

If now a normal complex is taken from each of the three leads, it can be seen that there is no left ventricular preponderance, confirming the clinical and roentgen findings. This accounts for the QRS complexes of the blocked impulses being not particularly pronounced.

The first efforts at direct investigation of disturbances in the conduction in the branches of the bundle of His arose after the work of Eppinger and Rothberger in 1910.[6] They injected silver nitrate into the muscle of the heart with the purpose of ascertaining what the effect of involving of a large area of the heart would be on the electrocardiogram. They were struck by the fact that in certain instances a marked disproportion existed between the amount of muscle involved and the electrocardiograph findings. If a small area were involved near the branches of the junctional system, a marked change was noted. They[7] followed this with experiments directed to cutting either branch of the bundle of His, and obtained curves characteristic of the lesion. Eppinger and Störk[8] then reported five cases in the human being in which two show post-mortem verification. The work was continued by Rothberger and Winterberg.[26] From then on until the present time the Viennese school have been intensely interested in conduction disturbances in the bundle of His and its branches.

Lewis[16] also obtained experimental corroboration and showed that the normal electrocardiogram was the algebraic summation of a dex-

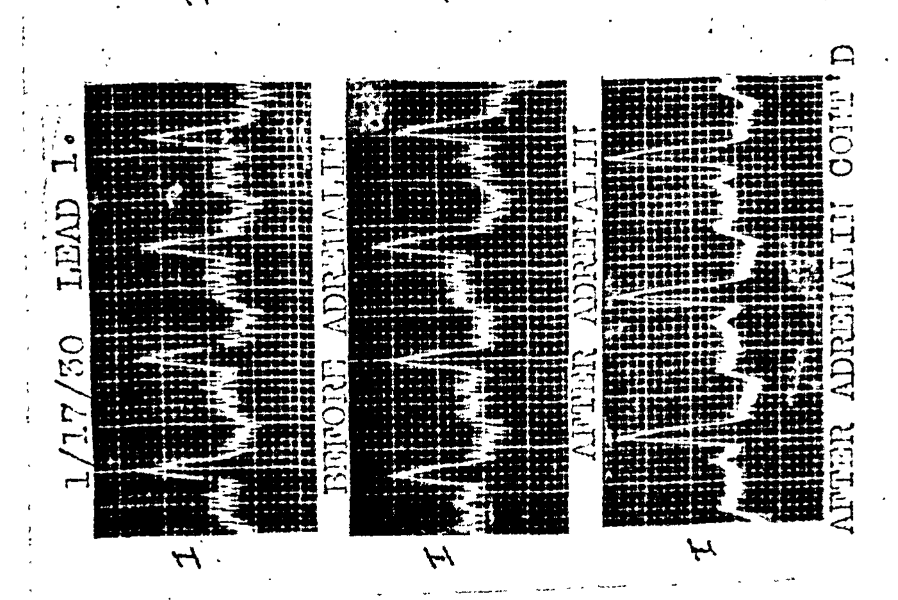

Fig. 6.

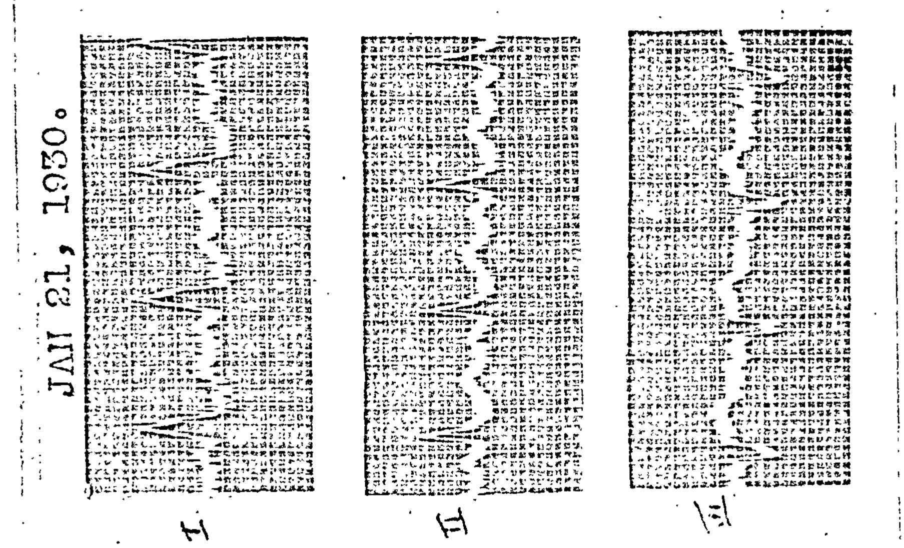

Fig. 7.

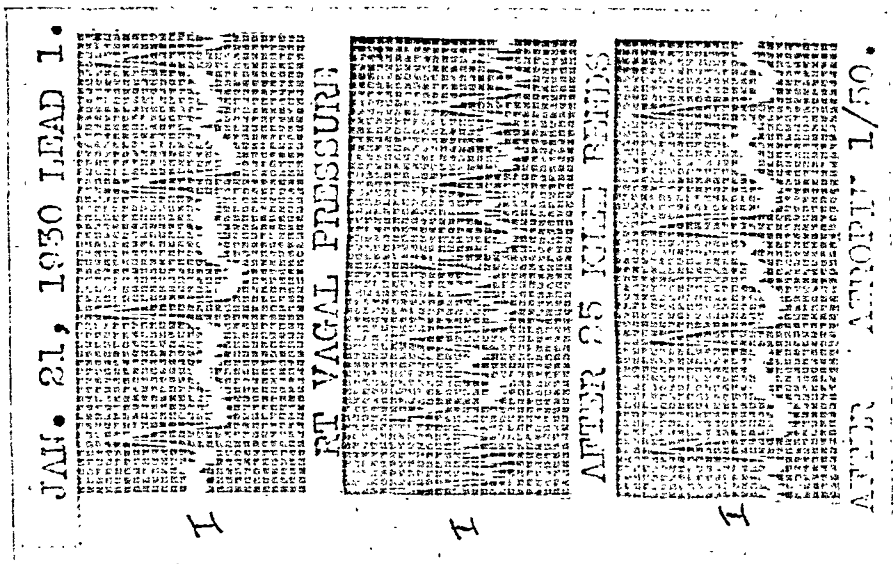

Fig. 8.

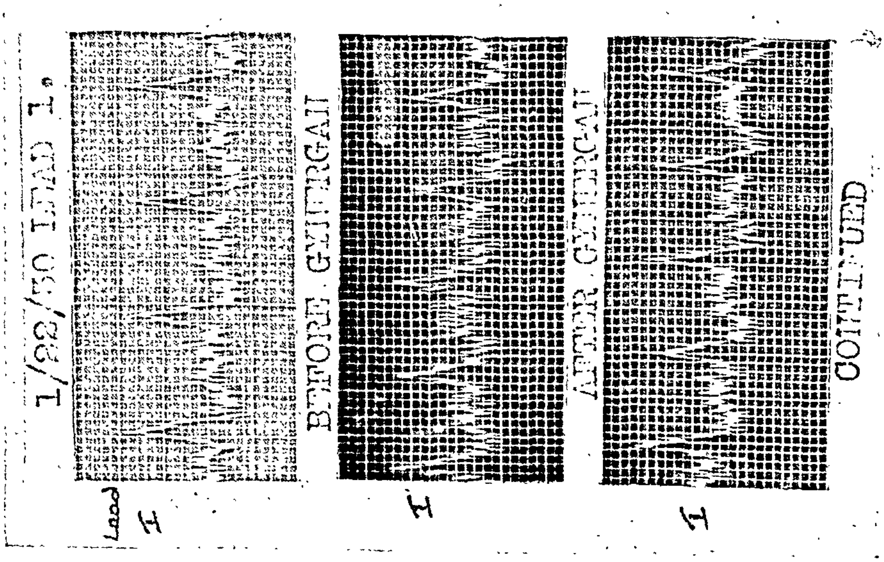

Fig. 9.

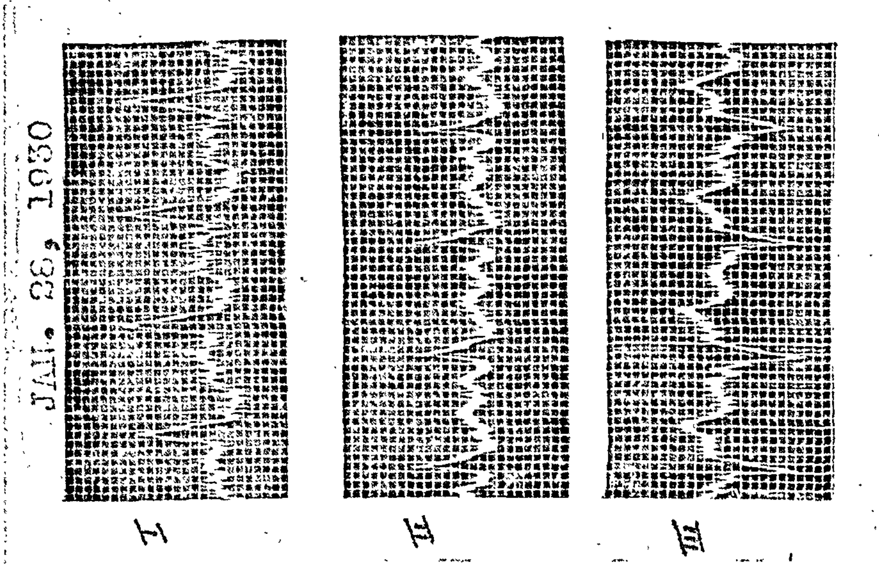

Fig. 10.

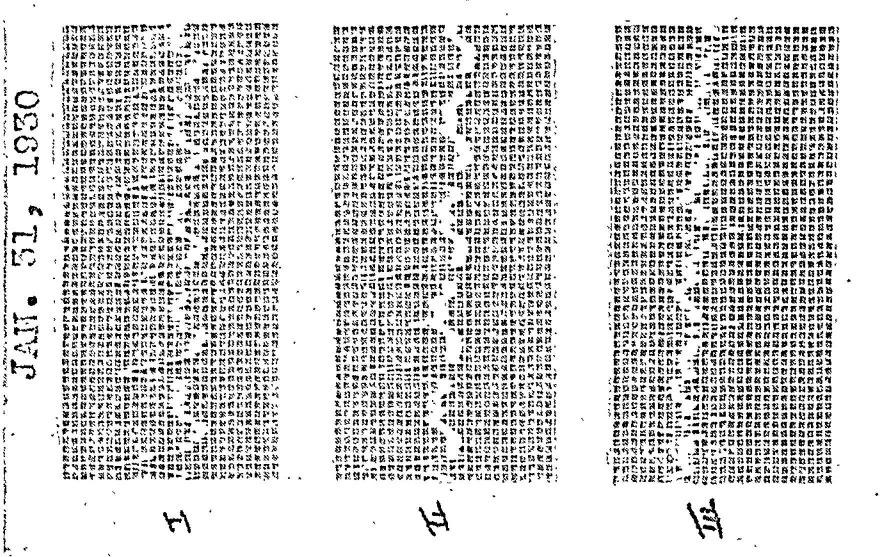

Fig. 11.

trocardiogram and a levocardiogram. At this time various papers of Christian,[2] Cohn,[4] Mathewson,[18] Fridericia and Möller,[9] Robinson[22, 23] and Wilson[34] aroused the keenest interest in the possibility of incomplete block of either branch of the bundle of His. This led to a most brilliant piece of experimental work on this phase of the question by Wilson and Herrmann.[36] Then Stenström[29] reported his first paper on incomplete bundle-branch block.

From then on tremendous clinical corroboration was obtained and the condition of bundle-branch block invited closer study, both experimental and clinical. It was then learned that blocks may occur in either branch which resemble auriculo-ventricular block. The work of Scherf[26] and Stenström[30] stands out.

Of the various classifications of A-V block, such as that of Wenckebach and Winterberg,[37] and Lewis, it is apparent that two broad divisions may occur. They are the complete block and the incomplete block. The incomplete auriculo-ventricular blocks are further subdivided into those without dropped beats and those with dropped beats. The latter, called partial heart-block, is again divided into those in which the dropped beats occur with a gradual increase of conduction time until a point is reached whereby the stimulus is completely blocked. The other type of dropped beats occurs without any warning so to speak; the conduction time is normal but a stimulus is suddenly blocked. This is the Hay's type. According to Mobitz, the latter is called type II heart-block.

This classification is necessary for the understanding of conduction disturbances in either branch of the bundle of His. I believe with the report of my case, *which is the first of its kind on record, not only clinically but also experimentally, to have filled in the last gap in the chain which completes the resemblance to auriculo-ventricular block.*

Blockage in the bundle can therefore be compared kind for kind and type for type with auriculo-ventricular block *with certain differences which I will explain further on. These differences are due to the anatomical arrangement of the bundles and the method of supply to the ventricles of the impulse. In order to clarify the above* classification, I will use *incomplete bundle-branch block* in the sense *of simple prolongation of conduction* as compared to a prolonged P-R interval, *partial bundle-branch block* for the dropped beats as compared to that in auriculo-ventricular partial heart-block with dropped beats. The partial bundle-branch block is further subdivided into those cases with gradual increase of conduction time and finally dropped beats, the so-called "Wenckebach Periods" and the dropped beats without prolongation of conduction time. Then there is the complete bundle-branch block.

CLASSIFICATION OF BUNDLE-BRANCH BLOCK

I. Incomplete bundle-branch block.
II. Partial bundle-branch block.
 A. With formation of "Wenckebach Periods."
 B. Without prolongation of conduction time (Type II, Mobitz).
III. Complete bundle-branch block.

Incomplete Bundle-Branch Block.

This type of bundle-branch block is compared to that of simple prolongation of the P-R interval in auriculo-ventricular block. It is characterized in its analogy by the increase in the QRS time. Some very important points should be mentioned at this point. When the impulse reaches the bifurcation of the bundle of His, it travels down each branch producing a dextrocardiogram and a levocardiogram which algebraically summated produced the normal electrocardiogram. If the passage is delayed in the slightest degree, the impress of the intact cardiogram dominates the picture. The delay in either branch of the impulse by as little as 0.005 second is sufficient to cause the electrocardiogram to change and begin to assume characteristics of the intact ventriculogram (Wilson and Herrmann[36]). In other words the normal electrocardiogram is divided into its two components more and more as the impulse is retarded in the diseased or the cut branch of the bundle of His. Now in the dog, as worked out by Lewis and Rothschild, by estimating the delay of the wave of negativity, they found a difference between the intact and severed ventricle of about 0.03 second. These figures corresponded to those of Wilson and Herrmann, who estimated in another way, that is, by the refractory period that the delay was the same. There is no direct way of estimating this in the human being. However, because of the larger heart and the longer system of branches of the bundle of His in the human being, we can estimate indirectly by the speed of conduction and the difference in length that the delay of the impulse in the ventricle with the severed bundle should reach between 0.035 and 0.05 second. This at the best is only a crude way and the results are not accurate.

If the conduction in either branch in the human being is delayed more than from 0.035 to 0.05 second, the picture produced on the electrocardiogram is that of complete bundle-branch block. The duration of the block, however, in the branch may be anywhere from 0.05 second to one second; for if the conduction time can be prolonged so greatly in auriculo-ventricular block (cases have been reported of that length) there seems no reason why such delay should not occur in either branch of the bundle of His. The anatomical distribution of the fibers and the heart itself causes this difference, however. If the impulse is delayed in either branch, the intact branch activates its

own ventricle and the other ventricle is activated through the septum indirectly. After from 0.035 to 0.05 second the injured ventricle has been completely though indirectly activated. Still its own bundle may be "passable"; that is, the impulses may be conducted through it, but by the time it could do it the impulse has passed from the intact ventricle through the septum and the injured ventricle already activated. The impulse, so to speak, is frustrated in the injured branch. Two important facts follow from this. First innumerable cases which are called complete bundle-branch block are in reality incomplete bundle-branch block. And secondly, there is a matter of only 0.035-0.05 second for the play of the various types of incomplete bundle-branch block as noted in the classification above to make itself manifest. This latter fact is what has made it so hard to find clinical examples of the various types of block to correspond to those of the A-V block.

With this in mind we must go back to the earliest descriptions of bundle-branch block. Lewis noted in auricular extrasystoles that very often there was an aberrancy of the ventricular complex. In addition it was later noted that in various types of auricular tachycardia, mostly in auricular flutter that the ventricular complex assumed an aberrant form. The work of Nils Stenström[29] should be mentioned in this place. In one of his cases with the beginning of the auricular tachycardia, the cardiogram was normal, but as the tachycardia continued the cardiogram assumed aberrancy. These clinical cases have been reported repeatedly. The aberrancy consisted in the ventricular complex assuming a form like that of a dextrocardiogram or a levocardiogram, which meant that in these cases there was either a delay or a complete block in either branch in the bundle of His. In auricular extrasystoles, its early occurrence or a slow recovery time in either branch, loaded this particular branch and conduction was blocked or delayed. The same applies to those cases of auricular flutter and tachycardia. It is difficult to state whether the impulse is delayed beyond the given time or whether the block is complete because in the electrocardiogram there are no definite criteria if the picture is that of complete bundle-branch block. This also applies to those cases in which there was bundle-branch block at one time (Willius and Keith[33] and Kapff[12]) and at a future time this had disappeared. We know that complete A-V block can recede. However logical it may appear to assume that if the block appears and disappears in very short intervals, we are dealing with incomplete heart-block, there is not the finality such as we would find in simple prolongation of the P-R interval.

But many cases have been reported of transitional forms between a normal cardiogram and a dextrocardiogram or levocardiogram. As is often seen in hospital records; there is widening but the T-wave does not make a diphasic curve. Or records are seen which look inter-

mediary, that is, there is not enough widening of the QRS with an inverted T, and subsequently, when a record is taken on the same patient, we now find a picture of complete bundle-branch block. Cases have been reported in which the vagus played an important rôle in delaying conduction in one of the branches of the bundle of His. In the course of vagal pressure the electrocardiogram took the form of bundle-branch block. Often intermediary pictures were obtained, only to recede quickly, which certainly indicated delay of conduction in one of the branches. In the beautiful pictures of Lutembacher[16, 17] where schematic representation of delay of one cardiogram in certain time increments produces variations in the cardiogram, the picture we often see in our own records can be found where the delay of conduction lies within 0.03 second.

Another point to be mentioned is that the so-called arborization block is being interpreted because of experimental corroboration[35, 36] as incomplete bundle-branch block.

Incomplete bundle-branch block is not at all uncommon and many cases of so-called complete bundle-branch block are only higher forms of incomplete bundle-branch block.

Partial Bundle-Branch Block.

If in conduction disturbances three factors and even a fourth are important, namely, the strength of the stimulus, the conductivity, the irritability and finally contractility, the classification is justified. In the division of partial heart-block or where there are dropped beats of two types, namely, the one with gradual increase of conduction time and then the drop of a beat and the other of dropped beats without prolongation of conduction time, it is possible that the factors above mentioned are of the utmost importance.

In comparing a growing P-R interval (Wenckebach Periods) until the drop of a beat with that of partial bundle-branch block of this type, we must remember that the QRS is comparable to the P-R. As conduction is delayed more and more in one branch, the QRS grows wider and wider because of the contralateral activation, until the full picture of a complete bundle-branch block is obtained. It is therefore necessary that in partial bundle-branch block of type I, that the QRS grow wider and wider until a complete dextrocardiogram or levocardiogram is obtained and then suddenly the next cardiogram is normal. This occurs because as the last impulse to the bundle was blocked, the bundle rested and the next impulse from the A-V node spread normally producing a normal cardiogram. Records of clinical cases have been reported (Christian[2] and Wilson[34]).

Cases of two-to-one partial bundle-branch block have been reported. The electrocardiogram shows a normal cardiogram followed by a dextrocardiogram or a levocardiogram with similar R-R periods. Three cases are mentioned in the textbook of Wenckebach and Winterberg,[37]

one by Stenström[31] and one by Leinbach and White.[13] In what light are we to interpret these? Are they of type I or type II? If there were a three-to-two block, it would be easy, for in the two curves which transmitted the impulse the growth of the QRS interval would show whether the so-called periods were being formed. But in two-to-one block this is not possible. So these cases might be of either type. In the case of Stenström[31] he shows records (see plates 18 and 19) in which there are two normal and one abnormal cardiogram and calls this a three-to-one block. This is a misnomer and he admits in his text that it may be so. It should be called two-to-three block. Let us compare this with A-V block. If it were of the type in which we have three auricular beats which produce two consecutive responses in the ventricle and a third beat is blocked, we should be dealing with a three-to-two block, that is one dropped beat. If the two responses of the ventricle show increasing P-R intervals before the dropped beat it is of type I partial heart-block. If the P-R is constant in the two transmitted beats and the third is dropped it is of type II. In Stenström's record only the third beat was dropped but two consecutive beats showed no increase in the QRS and the third beat which was blocked came without warning, so to speak. We are therefore dealing in just this isolated part of his record with a three-to-two partial bundle-branch block of type II.

This brings us to our record. It shows both three-to-one and four-to-one partial bundle-branch block. Two or three impulses are blocked in the right branch but a third or fourth is conducted through normally. The block shows intermittence. Immediately after the normal beat, without warning, the next two or three impulses in the right branch are blocked. If we compare this to A-V conduction, that is, the P-R interval is normal and then suddenly two or three auricular beats are completely blocked it would not belong to type I, for then there should be a growing QRS interval beginning with a normal or almost a normal QRS immediately after the conducted impulse. In our record this is not so. The QRS immediately after conduction is at once raised to that of all the others which are blocked. This case, therefore, belongs to type II of partial bundle-branch block and fulfills requirements mentioned by Wenckebach and Winterberg[37] at the bottom of page 360: "Intraventricular block of type II can on the other hand be confirmed when, without dropping of ventricular systoles, one normal electrocardiogram follows two or more similar atypical complexes. No known clinical example has come to our notice."

If the factor of irritability in this case is used, it might be possible to give some explanation of what has happened in this case. It would seem that the irritability was of a very low degree and when the impulse was conducted through the right branch, the threshold was raised

high enough by the previous rest to enable the impulse to pass. With the conduction, irritability was exhausted and a rest period of usually 1.712 seconds or occasionally 1.25 seconds was sufficient for the threshold to reach the height necessary for conduction again to take place. If in addition in this case the strength of the stimulus were low it would form an additional factor for the disturbance in conduction. This patient had myocardial involvement.

In an attempt to bring out conditions which might influence any of the factors of conduction the patient was submitted to various tests. However, they were all unsuccessful in improving conduction.

SUMMARY

1. A case of three-to-one and four-to-one partial bundle-branch block of type II is reported which we believe is the first of its kind in the literature.

2. Some phases of incomplete and partial bundle-branch block are briefly discussed.

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THE LOCAL AND SYSTEMIC EFFECTS OF ARTERIO-VENOUS FISTULA ON THE CIRCULATION IN MAN*

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INTRODUCTION

ONLY within recent years has it been realized what profound systemic effects acquired arterio-venous fistulae may exert on the human circulation. During the past decade, however, experimental and clinical studies by Reid,[1] Holman,[2] Matas,[3] Lewis and Drury[4] and others have demonstrated that such abnormal communications between the arterial and venous portions of the vascular circuit may so severely damage the heart and peripheral circulation that chronic invalidism and even death may result. It has, therefore, generally been conceded that operative interference for the relief of such fistulae is desirable not only to alleviate the local condition but also to avoid or remedy general circulatory failure.

Although much information has been gained as to the functional pathology of the circulation in this condition, the exact mechanism of many of the circulatory phenomena commonly observed is disputed. In particular, there has been little direct experimental study in man of changes in the cardiac output, in venous pressure, and in the circulation in tissues adjacent to the fistula. The purpose of this investigation was to repeat certain of the observations previously made and to obtain further knowledge of the circulatory changes in arterio-venous aneurism by the application of recently introduced technical procedures. In the cases here reported it was possible to study the effect on the circulation of suddenly eliminating the aneurism by manual compression. Moreover, both patients were carefully observed following operative excision of the fistulae. These post-operative observations throw objective light on the value of surgical elimination of the arterio-venous fistula. This unusual opportunity for observing patients in whom the whole circulation may be profoundly altered, either acutely by manual compression, or permanently by operation, makes the study of arterio-venous aneurism of especial importance. Such study may throw light on the physiology of the circulation in general, and, in particular, on types of cardiovascular disease presenting analagous circulatory phenomena.

The two cases of arterio-venous aneurism studied were similar in being of traumatic origin and of short duration. One patient had a fistula sufficiently extensive to produce the classical effects on the general cir-

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culation; the second showed no or slight systemic disturbance, but presented important local vascular changes. The clinical and experimental records of these patients will be presented separately.

Case I

(a) *Clinical History and Physical Findings.*—The patient (J. L.) was a butcher of 23 years whose family and past history was negative. Twenty-nine days before entry, on September 14, 1929, while cutting meat, he accidentally stabbed himself over the right femoral vessels. He lost a considerable amount of blood at the time and fainted. He was later transfused and remained in bed. He was weak from loss of blood; conscious of a pulsation in his right groin; and had considerable pain in his right leg and foot. This pain was particularly marked on holding the foot in a dependent position. There were slight cardiac symptoms. Examination revealed a well-developed but somewhat pale young man. The lungs showed no abnormality. There was marked pulsation in the carotid, brachial and radial arteries. The left border of the heart was just outside the nipple line. The sounds were loud and there was a systolic murmur at the apex which was also heard over the carotid and subclavian arteries. Both radial pulses were collapsing in quality and there was marked capillary pulsation. Over the right groin, below Poupart's ligament, there was an elevated pulsating area over which there was a continuous thrill and murmur with systolic accentuation. The thrill and murmurs also extended over a considerable area beyond the tumor, particularly downward, nearly to the knee. The skin surrounding the tumor was definitely warmer than on the unaffected side.

The patient remained in bed for three months in order to establish adequate collateral circulation. During this time his anemia diminished greatly. He was constantly aware of a forceful heart action. The pain in his right leg became less, but otherwise he showed no subjective or objective change. On December 5, 1929, Dr. William Morrison performed a quadruple ligation of the right femoral artery and vein, under ether anesthesia, and removed a saccular aneurism about four centimeters in diameter with an opening between the artery and vein about three millimeters in diameter. Following this, convalescence was uneventful except for slight infection in his wound. There was no evidence of deficient circulation of the right leg. The palpitation disappeared. Examination three weeks after operation showed that he was less pale than at the first examination. There was no capillary pulsation, nor visible pulsation of the peripheral arteries. A slight pistol shot was heard over the brachial and left femoral arteries. The left border of the heart was percussed the same distance from the sternum as formerly. The sounds were normal and no murmurs were heard over the heart or vessels of the neck. Over the right Scarpa's triangle there was a scar about five inches long in which were two small areas of infection. There was no tumor, thrill or murmur. The remainder of his convalescence was uneventful. Six weeks after operation he sat up and was discharged well three weeks later.

(b) *Circulatory Measurements.*—Certain of the circulatory measurements which were performed are tabulated in Table I. Where possible these measurements were repeated while the aneurism was completely occluded by manual compression over the fistula, and again following the operation. The figures given in many instances represent the average of repeated observations.

Pulse Rate.—Upon compression of the aneurism the heart rate per minute dropped from 80, which is slightly above the average normal for a man under basal conditions, to 60. This phenomenon of an immediate slowing of the cardiac rate upon occluding the fistula is generally known in this country as the Branham Bradycardia Phenomenon. The importance of this finding has been stressed not only

as a valuable diagnostic point in this condition, in particular as opposed to purely arterial aneurisms, but as an aid in evaluating the extent of existing systemic involvement.

Arterial Blood Pressure.—The measurement of the arterial blood pressure was accomplished both by a mercury sphygmomanometer and by a Tycos recording sphygmomanometer. The chief point of significance is the low diastolic pressure which was found. Upon occlusion of the aneurism there was a slight elevation of the systolic and a definite rise in the diastolic pressure, with a consequent increase in the mean pressure. Following operation, the average systolic pressure level was slightly lower than it had been previously, whereas the diastolic pressure had returned to a normal range.

TABLE I

CIRCULATORY MEASUREMENTS IN PATIENT 1

MEASUREMENTS		BEFORE OPERATION		FOLLOWING OPERATION
		ANEURISM OPEN	ANEURISM OCCLUDED	
Pulse Rate		80	60	74
Arterial Blood Pressure—Systolic	in mm. Hg.	120	127	115
Diastolic	in mm. Hg.	60	82	72
Venous Blood Pressure	in mm. Hg.	- 5		
Blood Volume	in c.c.	5400		
Cardiac Output per Minute	in L.	4.50	4.66	4.29
Arm to Face Circulation Rate	in sec.	20	18	19
Mean Velocity of Circulation	in sec.	72	77	
Alveolar Carbon Dioxide Tension	in mm. Hg.	42.3	44.8	44.4
Vital Capacity	in c.c.	4500		4500

Venous Pressure.—The venous pressure, determined according to the technique of Moritz and Tabora,[5] was normal. This is in accord with the findings of Lewis and Drury, and Matas. There have been few other direct measurements in man.

Blood Volume.—The blood volume was obtained by the dye method of Keith, Rowntree and Geraghty.[6] It represented 7.8 per cent of the body weight, which is within normal limits. The effect of a secondary anemia on blood volume is disputed,[7] both high and low values being reported. Further determinations were not performed, since the progressive increase in hemoglobin percentage, which this man showed, would prevent conclusions being drawn from any alteration in the blood volume which might have occurred. Holman[2] has adduced evidence to show that the blood volume is markedly increased in dogs in which arterio-venous anastomoses have been artificially created.

Cardiac Output and Velocity of Blood Flow.—The acetylene method of Grollman[8] was employed in calculating the cardiac minute-volume output. Table II gives in more detail the findings of cardiac output. For the estimation of the cardiac output with the aneurism occluded it was assumed that the oxygen consumption remained essentially unaltered during the time of the experiment. There is some basis for this assumption from experimental work of Lewis and Drury[4] and Harrison, Dock and Holman.[9]

Our results in determining the cardiac output in this subject are not conclusive, except in so far as they indicate that there was no great alteration of the volume flow through the heart. The acetylene method of Grollman which was utilized has been introduced too recently to be established as entirely reliable. Although we have employed it for some months, and our results have been fairly satisfactory, we are not yet ready to draw definite, final conclusions from it. In this particular patient, however, extremely consistent results were obtained. The figures for the cardiac output are within Grollman's normal standards[10] for a man of this size.

TABLE II

MEASUREMENTS OF CARDIAC OUTPUT IN PATIENT 1

DATE	PULSE RATE	ARTERIAL BLOOD PRESSURE		ARTERIO-VENOUS OXYGEN DIFFERENCE C.C. PER L.	OXYGEN CONSUMPTION C.C. PER MIN.	CARDIAC OUTPUT PER MINUTE L.	METABOLISM % OF NORMAL	REMARKS
		SYSTOLIC MM. HG.	DIASTOLIC MM. HG.					
10/29/29	82	120	60	56	260	4.67	+ 4.8	Aneurism open
	60	127	82	55	260	4.70	+ 4.8	Aneurism occluded
10/31/29	80			57	260	4.58	+ 4.8	Aneurism open
	62			56	260	4.62	+ 4.8	Aneurism occluded
12/ 3/29	78			65	281	4.35	+11.6	Aneurism open
12/26/29	82	115	70	70	274	3.90	+10.0	Following operation
				60	274	4.70	+10.0	
1/13/30	67	120	70	67	264	3.96	+ 4.8	
1/17/30	73	110	75	60	235	3.92	− 6.6	
				56	235	4.23	− 6.6	
1/23/30	74			60	282	4.67	+12.3	
				60	282	4.67	+12.3	

It may be claimed that what is measured when the aneurism is patent is not the total cardiac output but that portion of the cardiac output which does not pass through the aneurism. This is true if the blood which passes through the fistula returns to the lungs within the period of the technical procedure. We have reason to believe, from experimental work on the velocity of blood flow, that a relatively small amount of the blood passing through a femoral aneurism will reach the lungs within twenty-five seconds. However, it is probable that our results on the cardiac output with the aneurism open are somewhat too low and that actually the blood flow with the aneurism patent was greater than the flow during compression. Following excision of the fistula there was a tendency for the output to decrease slightly. A complicating factor in this patient was the anemia, for this in itself would tend to increase the cardiac output which would subsequently decrease with the return of the hemoglobin to normal.

Measurements of the velocity of blood flow from the arm to the face as estimated by the histamine method,[11] performed while the aneurism was open and occluded, and also following excision showed no change and were within normal limits.

Measurements were made of the carbon dioxide and oxygen content of arterial and venous blood obtained while the aneurism was open and compressed. The results obtained were too inconclusive to be of value as evidence and have not been recorded. The arterial oxygen capacity of this patient was determined, and rose from an average level of 14.0 volumes per cent before operation to 18.8 volumes per cent three weeks following operation.

(c) *Cardiac Size.*—By percussion and palpation there was questionable cardiac enlargement. A teleroentgenogram of the heart showed slight enlargement to the right, involving the auricle rather than the ventricle, but the total transverse diameter was within normal limits. At fluoroscopic examination, when pressure over the aneurism caused complete occlusion, a slight but distinct enlargement of the right auricle was observed. The border of the auricle moved from three to four millimeters to the right of its previous limits and was maintained there until the pressure was released. This observation was confirmed on repeated examination. One month following operation, the teleroentgenogram of the heart was repeated. At this time the cardiac measurements showed a slight decrease in all diameters from those previously observed.

(d) *Electrocardiogram.*—Electrocardiographic tracings were normal. When repeated with the fistula occluded there was a prolongation of the T-P interval consequent on the slowing of the heart rate, but otherwise no change was to be found, the electrical axis remaining essentially unaltered.

(e) *Skin Temperature.*—Observations of the skin temperature as determined with a thermocouple are recorded in Table III. The right thigh in the region of

TABLE III

SKIN TEMPERATURE MEASUREMENTS IN PATIENT 1

SITE OF MEASUREMENT	SKIN TEMPERATURE READINGS IN DEGREES CENTIGRADE	
	RIGHT	LEFT
Shoulder	32.9	32.9
Abdomen	34.1	34.0
Thigh—above aneurism	34.3	34.7
Thigh—over aneurism	33.9	33.3
Thigh—lateral to aneurism	32.2	32.0
Thigh—medial to aneurism	33.5	33.5
Mid-Thigh	33.8	32.7
Thigh—above knee	33.1	31.9
Lower Leg—below knee	32.9	32.3
Lower Leg—midportion	32.5	31.5
Ankle	33.2	31.5

the aneurism and below it showed a slight tendency to be warmer than the left, and skin temperature measurement over the right lower leg was definitely higher than over corresponding points on the left.

Case II

(a) *Clinical History and Physical Findings.*—This patient (A. C.) was a 25-year-old automobile mechanic whose family and past history was negative. He entered the hospital on October 24, 1929, with the story that five weeks before entry he had been injured in the left wrist by a flying chip of steel. He lost about half a pint of blood before a tourniquet was applied. When this was removed three quarters of an hour later there was no bleeding. The wrist was bandaged for a week and on removing the bandage he noticed a swelling in his wrist which pulsated and gave a thrill. There were no subjective sensations or incapacity, but he had not worked. Physical examination was negative except for the left arm. The lungs showed no abnormality. The cardiac size was well within normal limits and there were no murmurs. At the left wrist over the region of the radial artery, there was an expansile swelling, two centimeters in diameter, over which there was a continuous thrill and murmur with systolic accentuation. For about five centimeters above the swelling the radial artery was very easily palpable, seemed larger than normal, and pulsated more forcibly than on the right. The veins over the internal aspect of the left wrist and forearm were dilated, very prominent, and pulsated, but on raising the arm, collapsed well within normal limits at the same level as those on the right. There were a thrill, pistol shot, and Duroziez's sign over the left brachial artery but not elsewhere. The thrill and Duroziez's sign disappeared instantly on occlusion of the fistula, but the pistol shot persisted though diminished. Capillary pulsation was present to a slight degree beneath the finger nails of the left hand.

Three weeks after entry he was operated upon by Dr. H. B. Loder. A quadruple ligation of the left radial artery and vein was performed, and the aneurismal sac removed. This sac was about two centimeters in diameter with a communication between the artery and vein from one to two millimeters in diameter. Following operation there was no evidence of any circulatory embarrassment to the left hand, but there was an area of partial anasthesia and hyperesthesia over the left thenar eminence. On examination one month following operation he stated that he felt well but had not returned to work. General physical examination was negative. There was no capillary pulse and no pistol shot or Duroziez's sign over any vessel. Both arms appeared to be of equal warmth. There was no atrophy, change in color or loss of power in either arm or hand. At the left wrist on the radial side there was a linear scar five centimeters long which was sensitive to touch. Over the external aspect of the thenar eminence, and extending to include the scar was an area of diminished sensitivity to touch. There was no evident dilatation of the veins of the left arm and hand, and the radial artery above the scar could be felt pulsating and seemed of normal size.

(b) *Circulatory Measurements.*—The pulse rate per minute was 63. When the fistula was compressed there was a slowing to 59. Following operation the pulse rate was 56. The arterial blood pressure in the left arm was 107 millimeters of mercury systolic and 37 mm. diastolic before compression and 110 systolic and 35 diastolic following occlusion. In the right arm the pressure was 100 systolic and 50 diastolic both with the aneurism open and closed. Following operation the blood pressure was 100 systolic and 65 diastolic in each arm. It is notable in this case that there was little systemic alteration in the blood pressure and the general blood pressure was unaffected by occlusion of the fistula. However, the pressure in the artery proximal to the lesion showed a definite lowering of the

diastolic level, and this low diastolic pressure showed no tendency to return to normal when the aneurism was compressed. There must, therefore, have been a decrease in the peripheral resistance in the left arm which was not dependent on the abnormal arterio-venous communication.

(c) *Skin Temperature.*—Measurements of the skin temperature over both forearm and hands are recorded in Table IV. It is to be noted that the skin temperature both proximal and distal to the aneurism on the left was definitely higher than on the right arm. Moreover, the rise in skin temperature was maintained even when the fistula was compressed. This must have been due to an increased blood flow through the arm as a result of a lowered peripheral resistance unrelated to the fistula, in other words, an arteriolar dilatation. One month following operation skin temperature measurements over the two arms were equal.

TABLE IV

SKIN TEMPERATURE MEASUREMENTS IN PATIENT 2

SITE OF MEASUREMENT	SKIN TEMPERATURE MEASUREMENTS IN DEGREES CENTRIGRADE			
	BEFORE OPERATION		FOLLOWING OPERATION	
	RIGHT	LEFT	RIGHT	LEFT
Above Elbow—lateral	31.4	33.5	29.2	29.2
Below Elbow—medial	29.9	34.2	29.9	30.2
Mid-Forearm—lateral	29.5	31.3	29.5	29.4
Mid-Forearm—medial	29.8	34.1	29.9	30.4
Wrist—lateral (over aneurism on left)	29.7	34.3	30.9	29.5
Wrist—medial	28.7	33.3	31.1	31.7
Thenar Eminence	28.8	31.6	30.3	29.7
Hypothenar Eminence	27.8	31.6	31.1	31.4
Palm of Hand	29.5	32.7	31.4	32.0

(d) *Tourniquet Test.*—The total blood supply to the left arm was suddenly occluded while the arm was held upright to facilitate venous return. The arm was then lowered and with the fistula compressed immediately the tourniquet was released. A sudden and intense flush appeared over the ulnar and median aspects of the hand and forearm. The radial aspect of the hand became pink more slowly. When the radial artery was released, the thenar eminence immediately became pink.

When the test was repeated over the right arm, the color returned to the arm and hand more slowly and less intensely than it did on the left, a fact which the patient noticed and commented upon. Since the returning inflow of blood was able to reach the minute skin vessels of the left arm very much more quickly than those of the normal arm, this test, too, suggests that there must have been an arteriolar relaxation in the left arm. Moreover, this dilatation was unaffected by mechanical occlusion of the fistula.

(e) *Carbon Dioxide and Oxygen Content of Arterial and Venous Blood.*—The content of carbon dioxide and oxygen from the antecubital veins of both arms and of arterial blood is recorded in Table V. The blood from the left antecubital vein closely approached the arterial blood in character, whether the aneurism was patent or occluded. To obtain the sample following occlusion the arm was first held upright for one minute after compression of the aneurism in order to drain the blood from the veins. This experiment was repeated subsequently with identical results. Since there is no reason to believe that the metabolism of the two arms differed, the decreased oxygen utilization in the left arm must have been due to an increased blood flow in this region. Following operation the venous blood from both arms showed a normal content of carbon dioxide and oxygen.

TABLE V

DETERMINATION OF THE CARBON DIOXIDE AND OXYGEN CONTENT OF ARTERIAL AND VENOUS BLOOD FROM PATIENT 2

BLOOD FROM	PRE-OPERATIVE		4 WEEKS POST-OPERATIVE	
	CARBON DIOXIDE VOL. %	OXYGEN VOL. %	CARBON DIOXIDE VOL. %	OXYGEN VOL. %
,eft Antecubital Vein—aneurism open	47.76	18.96		
,eft Antecubital Vein—aneurism occluded	47.68	18.75	54.72	12.82
Right Antecubital Vein	54.39	12.24	55.62	12.65
Artery	47.28	19.51		

To summarize, evidence from four sources has been presented in this case of a lowering of the peripheral resistance in the neighborhood of the arteriovenous fistula. This lowered peripheral resistance is not due directly to the arterial leak, but to a generalized relaxation of the vessels where the resistance is normally highest; in other words, an arteriolar dilatation. The cause of the production of this dilatation will be considered later.

DISCUSSION

These two cases are of interest because, although both presented the characteristic local signs of an abnormal arterio-venous communication, they were dissimilar as regards the systemic circulatory manifestations. Matas[3] cites seven factors which are of importance in determining the effect of the fistula on the general circulation. These are: (a) the size of the fistula; (b) the volume and force of the arterial stream which is short-circuited; (c) the calibre of the vessels involved; (d) the proximity of the fistula to the heart; (e) the duration of the condition; (f) the age of the patient; and (g) the presence or absence of co-existent heart disease. In both cases here reported, the patients were young with previously normal cardiovascular systems and the fistulae were of short duration. However, in the first subject the fistula was of somewhat greater size than in the second, the volume of blood short-circuited was presumably greater, and the vessels involved were the femoral, of large calibre and relatively close to the heart, instead of the more peripherally situated radial vessels in the second patient. It is, therefore, natural to expect that the first man should show definite and the second very slight systemic effects.

Heart Rate.—A slowing of the heart rate upon compression of the aneurism was observed in both patients, although only slightly in the second case. Lewis and Drury[4] found that this effect was abolished by atropinization, and, therefore, attributed it to a vagal reflex initiated by the rise in mean arterial pressure. Rieder,[12] however, was able to elicit the slowing even after the injection of atropine, although the dosage which he employed was only half that given by Lewis. Rieder was also able to obtain the bradycardiac effect in dogs following division of the vagi. It is possible that there may be cardio-inhibitory

fibers, parasympathetic in nature, other than those which are contained in the vagus nerves. In the light of the recent work on the importance of the carotid sinus in the regulation of heart rate and blood pressure by Hering,[13] Heymans[14] and others, it is possible to advance two theories to account for the production of this reflex. First, the sudden increase in mean arterial blood pressure which occurs upon occlusion of the fistula may initiate the reflex in the carotid sinus itself. Second, the aneurism itself may locally assume a regulatory function such as is known to be possessed normally by the carotid sinus, and, upon the sudden alteration of the pressure in it or over it, be the starting point for a nervous reflex which terminates in cardiac inhibition. The pathway through which this reflex may travel is not clear. It has been shown[15] that spinal anesthesia does not abolish the phenomenon.

Cardiac Output.—Lewis and Drury[4] claim that there is no significant increase in cardiac output in the presence of an arterio-venous aneurism. They base this assumption on their inability to find an increase in general venous pressure, and on the experimental production of fistulae in dogs in which, in the absence of a rise in venous pressure, they were unable to detect any appreciable change in the cardiac output per minute. The mere fact that there is no increase in venous pressure appears to be an inadequate criterion for concluding that the volume flow through the heart is unaltered. While the systolic output does indeed depend on the venous return to the heart, it is possible that a heart with normal functional capacity responds so immediately to a relatively small augmentation of the venous return that it is impossible to detect clinically any rise in venous pressure. Indeed, clinical observations in certain conditions where the cardiac output is known to be increased, for example in hyperthyroidism, frequently fail to reveal an increased venous pressure. In arterio-venous fistula, it would appear quite possible for the cardiac output to increase without a demonstrable increase in venous pressure, provided the heart functions normally and the lesion is of sufficient duration to enable the circulation to have adapted itself to the altered conditions.

As opposed to the findings of Lewis and Drury, Harrison, Dock, and Holman[9] have presented evidence of an increase in cardiac output in dogs in which arterio-venous anastomoses had been produced experimentally. In their work the venous pressure was not measured, and it must be appreciated that the fistulae which were created were of a relatively large size.

In Case I no change in the cardiac output per minute was found when the fistula was acutely compressed, although for reasons already discussed these measurements may not have represented the total volume flow. Following operation when the circulation had readjusted itself to normal conditions, the volume flow showed a tendency to decrease somewhat, but the decrease in the anemia in itself might have been a

factor in the decrease in heart output. No conclusive evidence was obtained, therefore, that in this particular patient the arterio-venous aneurism increased the cardiac output greatly. In other patients with aneurisms of more considerable extent it is reasonable to believe that the heart output may show a marked rise. It is also probable that the cardiac output in cases of arterio-venous aneurism may be influenced according to whether the patient performs a normal amount of work, or as in Case I, the patient is resting in bed following the development of the fistula.

Peripheral Resistance.—From anatomical and physiological considerations, one cause for the lowered peripheral resistance occurring in arterio-venous aneurism can be found in the direct short-circuiting of the blood stream from an artery to a large vein. This must be so because not only are the physiological manifestations of a lowered resistance, particularly a reduced diastolic blood pressure, approximately in proportion to the extent of the communication, but many of these abnormal phenomena can be immediately abolished by compression of the fistula.

From the studies made on our second case, however, definite evidence was obtained that there was a lowering of the peripheral resistance, unconnected with the actual fistula, in other words, an arteriolar relaxation. The exact nature of the production of the dilatation cannot be explained conclusively, but it is certain that it is related in some way to the abnormal circulatory conditions consequent on the arterial leak. There are certain possible factors, any one or a combination of which may be etiologically responsible. First, there is the local damage to the vessel wall itself in the fistula as well as the widening of the artery proximal to it. These factors seem unlikely as the cause when one considers the extensive vascular damage, particularly in pure arterial aneurisms, which may occur without reflex arteriolar dilatation. Second, the stretching and engorgement of the veins communicating with the fistula might initiate such a reflex. When veins are thus engorged with blood under a relatively high pressure there is a retrograde pressure in the capillaries and a tendency for capillary blood flow to cease. Reflexly, then, the arterioles might dilate in an endeavor to maintain the normal capillary circulation. A third explanation, also, can be given for the diffuse arteriolar relaxation. The increased pulse pressure, with its resulting lowering of the mean arterial pressure, which has already been produced by the fistula, may produce the arteriolar dilatation in an endeavor to maintain the capillary pressure at the normal level which is essential for the adequate exchange of gases between tissues and blood. These possible mechanisms of the production of the lowered peripheral resistance have been presented as theories only. The question is an open one and awaits further investigation.

It is possible that this regional vascular dilatation may play a rôle in what is known as "the establishment of collateral circulation." In

particular, this phenomenon may serve a purpose in maintaining an adequate blood flow to the tissues until the time when the regional vessels have become permanently enlarged. We have shown that an arteriolar dilatation may occur in conjunction with arterio-venous aneurism. In cases showing fistulae of greater size, may this arteriolar dilatation be more extensive, even generalized, and contribute to some of the systemic effects which are observed? The problem of attempting to demonstrate this is complicated by the fact that a direct lowering of the peripheral resistance through the arterio-venous shunt is a very important, if not the major, factor in producing the systemic manifestations. Any attempts to exclude this factor by temporary compression of the aneurism result in a serious altering of the physiological conditions from those to which the circulation has already become adapted by redistribution of the blood volume, changes in the cardiac output, etc. For this reason, the influence of an arteriolar dilatation may not be readily discernible. One phenomenon, however, which is commonly seen in cases of arterio-venous fistula, and which is uninfluenced by temporary compression of the communication, is that of "capillary pulsation." This was observed in our first patient, and was also commented upon by Lewis and Drury.[4] Lewis[16] has recently presented definite evidence that this phenomenon is in truth occasioned by an arteriolar dilatation. If, therefore, capillary pulsation does indicate an arteriolar relaxation, as seems highly probable, there are excellent grounds for the belief that an arterio-venous aneurism may produce a generalized arteriolar dilatation as well as the local dilatation which we have shown does occur.

It is quite possible, moreover, that such a reflex lowering of the peripheral resistance may exist in certain other clinical conditions in which the circulatory manifestations are somewhat similar to arterio-venous aneurism. In particular, this may be true in aortic insufficiency. Lewis and Drury concluded, as a result of their investigation of arterio-venous aneurism, that in aortic regurgitation, the amount of blood regurgitating into the left ventricle must be a significant quantity. This is in opposition to the view first advanced by Stewart[17] that the quantity of regurgitating blood is trivial and that the peripheral circulatory manifestations are the result of a reflex lowering of the peripheral resistance. As stated previously, we believe that the criteria upon which Lewis and Drury base their assumption that the cardiac output in arterio-venous fistula is unaltered are inadequate, and we also believe that there is evidence, both theoretical and experimental, that the cardiac output may be increased in arterio-venous fistula. Our investigation has thrown no light on the question as to whether or not the amount of regurgitating blood in aortic reflux is significant. However, since evidence has been presented by us that a generalized lowering of the peripheral vascular resistance may exist in cases of arterio-venous

aneurism of moderate size, it is very suggestive that in aortic insufficiency, which presents analogous peripheral circulatory phenomena, including capillary pulsation, there may also be a diminution of the peripheral resistance.

To sum up: an arterio-venous aneurism produces characteristic local signs and symptoms which are too well known to detail here. It also may be responsible for certain general effects on the circulation, which vary in their occurrence and extent with the size and location of the fistula. The most characteristic of these phenomena are, (a) an increase of the heart rate, with an immediate slowing upon compression of the aneurism; (b) a decrease in the diastolic arterial blood pressure, with a resulting increased pulse pressure; (c) cardiac enlargement; (d) a redistribution of the blood volume with a tendency toward an accumulation of blood in the venous portion of the vascular circuit, and probably an increase in the total blood mass; (e) a normal or possibly increased cardiac output, depending on the degree of fistula; (f) a regional and frequently a generalized arteriolar dilatation.

In our first patient, the general effects of the lesion were apparent but not marked. This may have been due to the comparatively small size of the fistula. However, it was 3-4 millimeters in diameter, which is as large as the internal diameter of the brachial artery, and must have conveyed a considerable amount of blood. The fact that this man was at absolute rest between the time of his injury and operation may explain to a certain extent the lack of more marked systemic involvement. We believe that patients with arterio-venous fistulae showing such systemic effects should have the benefit of as complete rest as possible in order to spare their general cardiovascular system, and that operative excision of the lesion should be performed in every case without undue delay.

SUMMARY

1. Two cases of traumatic arterio-venous fistula were studied before and after surgical operation. Both patients showed the characteristic local signs of the condition, and the first patient presented the classical phenomena of the effect on the general circulation.

2. In the first patient estimations of the cardiac output were performed, and although the applicability of the method is somewhat limited in this condition, the measurements showed no marked change upon compression of the aneurism and a slight tendency for a decrease following operation. The velocity of blood flow in this subject showed no change at any time. The blood volume was normal.

3. Evidence was presented of an arteriolar dilatation in the surrounding region of the arterio-venous aneurism in the second patient.

4. It was suggested that in certain cases of arterio-venous aneurism of marked extent, the arteriolar dilatation may be generalized. Likewise, in aortic insufficiency such an arteriolar dilatation may exist. This

would explain the capillary pulsation and to a certain extent other of the peripheral circulatory phenomena which are observed both in arterio-venous fistula and aortic regurgitation.

We take pleasure in expressing our appreciation of Miss Rose Shore's technical assistance in conducting this research.

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CARDIAC SYMPTOMS NOT DUE TO CARDIAC DISEASE

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CONFUSED and fantastic though the layman's knowledge of anatomy may be, he invariably knows where his heart is located and with rare exception, attributes every unusual sensation in this region to disease of that viscus. The fact that not infrequently it is impossible to detect serious disease of the heart even with the aid of instruments of precision, justifies the apprehension that pain in this region occasions.

I have recently had the opportunity of studying two patients presenting cardiac symptoms due to extra-cardiac causes that puzzled me greatly for some time. In one, pain over the precordium was the chief complaint; the other suffered from attacks of palpitation, the cause of which was only revealed when the early emotional life of the patient was carefully investigated.

CASE 1.—D. D., an unmarried woman, aged 25 years, who was employed painting dials on clocks with radium, was admitted to the Hartford Hospital October 8, 1928, complaining of pain about the heart and stomach. The former pain had been present several years and was the more severe. It would come on suddenly, last an hour or all day and would not radiate. It was located internal to the cardiac apex. The other pain was behind and below the lower end of the sternum and was not affected by food but was sometimes relieved by alkalies which, however, never relieved the precordial pain. The patient had lost considerable weight and suffered somewhat from dyspnea and palpitation.

The important physical findings and laboratory data were as follows: She was a tall slender girl with marked reduction of antero-posterior diameter of the chest; slight enlargement of thyroid isthmus; heart not enlarged, but a loud harsh systolic murmur was heard all over the precordium, loudest internal to the apex.

Left knee reflex not obtained; right elicitated only with reenforcement: Hb., 64 per cent; R.B.C., 3,420,000; W.B.C., 6100 (64 per cent lymphocytes); blood culture, Wassermann test and stool all negative. Roentgenography of the gastrointestinal tract was negative for ulcer but showed a slight six-hour stasis. Basal metabolism rate was −10 per cent; temperature and pulse were normal. Notwithstanding a negative history of rheumatism, I feared that she probably had an old rheumatic mitral valve lesion and that the pain probably indicated activity. The pain behind and below the lower part of the sternum was at first thought to be probably due to a peptic ulcer even though this diagnosis was not substantiated by the radiological examination. Both of these assumptions proved wrong.

One consultant thought that the pain was perhaps due to pressure from the thyroid. When first seen, the possibility of poisoning from radium was uppermost in our minds. There was moderate secondary anemia but a normal leukocyte and differential count. A few months later, Dr. Frederick B. Flynn, of Columbia University, gave her the electroscopic and expired air tests, which will detect as small

an amount as two micrograms of radium, with negative results. The change in the knee reflexes was of temporary nature.

The precordial pain promptly subsided upon rest in bed and the institution of the Sippy régime for ulcer seemed to control the epigastric pain but when the patient began to get up after three weeks, preparatory to going home, both pains recurred as severely as before. Our mutual disappointment was great. I then did what I should have done three weeks previously, examined her in a standing position. She stood with markedly drooping shoulders, protuberent abdomen and greatly exaggerated lumbar lordosis. When sitting, she slouched with shoulders forward. Believing that the pain might be the result of faulty posture either from radicular irritation or pinching of the intercostal nerves by approximation of the ribs anteriorly, her shoulders were strapped back with adhesive plaster and the abdomen supported in like manner. This assumption proved to be correct as she was at once relieved from pain. Inquiry then revealed that in the factory she worked at a low table and as she was above the average height, she had to sit stooped forward all day. She was instructed to bend forward from the hips, keeping the spinal column straight. Upon her return to the factory, the worktable was raised and she has now worked several months without pain. Once or twice when there was a suggestion of the old pain, she stopped it at once by correcting her posture.

COMMENT

The patient's disability was occupational in nature; not, however, due to the fact that she was using radium but to the position she assumed while using it. Had the patient been examined in the office, her bad posture would undoubtedly have been detected at the first consultation but as she was in bed when first seen, she was not examined standing until several weeks had passed. No patient can be considered to have had a complete examination until observed in the sitting and standing positions. If the patient be a machine operator for instance, a great deal of light is often thrown on an obscure pain if one observes the posture assumed while he performs the various motions used in operating the machine. Within a few weeks, a slender girl who worked as a cashier, consulted me because of precordial pain especially marked in the late afternoon. No organic cause was found but it was readily apparent her posture was very poor. The cause of the pain was explained to her and she was instructed how to maintain a correct posture. One week later she said she had had no recurrence of the pain. Several similar cases have been seen. Neither Levy[1] nor White and Wood[2] in their recent contributions on cardiac pain, refer to bad posture as a cause. The latter authors, speaking of simple fatigue pain state that "It may be the result of a number of different factors." Gunther and Sampson,[3] in discussing the pain referred to the precordial region, due they believed to radicular irritation the result of hypertrophic spondylitis, state, "The intensity of symptoms does not parallel the degree of anatomic changes shown by roentgen examination. It is evident that their symptoms depend not only on the mechanical factors mentioned but on others which at present are not so clear."

It would seem that the mechanical factors might be especially prone to be operative when the upper segment of the spine is strongly flexed, as occurs with the slouching posture. Hypertrophic spondylitis is rare in early life but common past middle age. Garvin[4] in the study of 2,000 radiograms at the Mayo Clinic found evidence of hypertrophic spondylitis in 67 per cent of men and 40 per cent of women over fifty but in 74 per cent of the former and 61 per cent of the latter it appeared to cause no symptoms.

Gunther and Sampson noted in their patients that the pain might be absent on arising in the morning, due they believed to increase in the tonus of the paravertebral muscles. Obviously, the effect of the increase in muscle tone enables the individual to hold himself more erect and consequently he has less pain. The return of the pain on prolonged sitting must be due to the increase in the forward bending of the spine as the individual slumps. Adhesive strapping to hold back the shoulders for a week, instruction how to walk and sit, together with exercise to develop the spinal muscles will promptly effect a cure if posture be the cause.

CASE 2.—Viola B., aged 27 years, married, was admitted to the Hartford Hospital because of attacks of palpitation. The attacks began in childhood and have occurred especially at night. With these attacks she "gets cold all over" and her heart "pounds" very hard. They come about once in two or three weeks though for a time when the patient was about 16 years old, they were almost daily. Seven years ago she married and went to Florida to live and while there, the attacks were very rare—only once a year. She left her husband one year ago because of his bad habits. Two children are living and well. For the past two years she has spent the summer north with her parents and at these times the attacks have been much more frequent, often awaking her in the night. She feels "dopy" and is tired after them but has no pain at any time. As she has to earn her living, the attacks greatly interfere with her work and she fears she has heart trouble.

She was an attractive young woman who, aside from being slightly undernourished, had a negative examination except for a rather low metabolism rate (−19 per cent). Thyroid administration did not improve the situation. At first I attributed the attacks to her separation from her husband, especially as they were rather more often at night. "How do you explain the fact" said she, "that I lived without him for a year in Florida with only a very rare attack and have had frequent attacks when living with my father and mother who try to do everything for me"? It was some time before I could answer her question and though I told her they were not serious, I could not convince her until I was able to explain them.

Was the increase in the number of attacks when with her parents an indication of a desire on her part for attention and solicitude? She was an only child and though very attractive physically, she had not been able to hold her husband's affection. Did the attacks signify a "bid" for parental solicitude?

It is quite common to see illness used as a means of obtaining attention and this possibility might explain the present attacks but would they explain those that occurred in early childhood?

As they began when she was seven years old, I finally asked her in detail about her childhood. I learned it had not been happy because of her father's alcoholism. He would get very drunk and be very abusive. He frequently threw dishes about,

shouted in loud tones and threatened to kill both mother and daughter. She would often go to bed too frightened to sleep and at these times, when she thought he might be coming in to carry out his threat, the attacks of palpitation had their inception. Her father reformed many years ago and the family is now a happy one but the patient said when she recently returned home she could hardly bear the sight of the household furnishings. Her grandmother's picture hung on the wall: she had no ill feelings against her but it looked down at her years ago when she was a terrified child and she dreads to look at it now: so it was with some of the dinner dishes. It seems as if she could not eat from the dishes remaining from the set from which her father had selected missiles to terrify the family in the years gone by. "I told mother," said she, "I believed I would be better if we got rid of all the old things." I suggested that as her father was no longer a drunkard, the furnishings of the house should remind her, not of the terrifying scenes of childhood but of the victory her father had won. She was further told that as she had had so many attacks in childhood, the mechanism that started them became so sensitive that it would sometimes be set going without any discernible cause. This explanation seemed to appeal to her and the attacks of palpitation became much less frequent and did not cause her the anxiety they had formerly occasioned.

COMMENT

This case illustrates how important it is to secure emotional data in obtaining a medical history. It is probable that "painful memories, present dilemmas and fears regarding the future" (Favill) cause as much suffering as, if not actually more than, organic disease. The sympathetic physician who takes the necessary time to study the emotional background of his patients is amply rewarded for his pains.

SUMMARY

Symptoms referable to the region of the heart, especially occurring in early life, are often not due to cardiac disease. Two illustrative cases are here presented. In one—pain was due to faulty posture assumed at work; in the other attacks of palpitation owed their inception to a long-continued state of terror in early childhood.

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HEART DISEASE IN THE STATE OF NEW YORK. A STATISTICAL REVIEW OF MORTALITY AND MORBIDITY*

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OUR mechanical age is a rapid succession of conquests over nature. The plots of Old World fairy tales and of dime novels in this country, in which a thing is "no sooner said than done," have become in the popular philosophy of the day, almost a reality. In our pride over material gains, we are in danger of overlooking the permanent values of human progress. Even some of our universities not infrequently speak in the language of real estate promoters and business boosters. While money undoubtedly facilitates scientific research, one must remember that there is no direct relation between the sums expended and the degree of success of the research. The scientific worker must guard against the prevalent conception of life. The motivating force in his work should be an urge for truth irrespective of its immediate or even ultimate utilization.

Although vital statistics is largely a practical method, a certain degree of detachment in the collection of the data and formulation of conclusions is, in my opinion, as essential here as it is in the pure sciences. The field of vital statistics is practically limitless. Everything and anything that affects the life and physical well-being of individuals and communities usually can be and frequently is expressed in numerical terms, out of which are built the prosaic-looking statistical tables. Only one or two generations ago statistical expressions were frequently guesses, or at best, rough approximations to reality. In those days, when some cities took great satisfaction in announcing death rates of 1 or 2 per thousand, and in one historic instance of a fraction of a point, even a poorly equipped but earnest prospector had comparatively little difficulty in uncovering nuggets of fact. We have now reached a stage where the search for truth requires more concentrated thought and greater refinement of tools. We must sink our wells deeper, we must work ores whose yield is little when compared with earlier and more prosperous days.

MORTALITY FROM HEART DISEASE

Of late years there has been considerable alarm over the high mortality from heart disease and especially its upward trend. If figures were infallible the alarm would be only too natural. In the State of

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New York, for example, heart disease has been the leading cause of death since 1912, with the single exception of 1918, when pneumonia held first place with a death rate of 337.5 per 100,000 population, followed by influenza (259.1); heart disease being third (239.0). In 1928 the death rate from heart disease was the highest ever recorded (297.9) and the deaths ascribed to this group of causes were responsible for almost one-fourth of all deaths (22.8 per cent).

The importance of heart disease as a cause of death increases with age. In 1928, in the entire State, it was sixth among the causes of death of children under 10 years of age who had weathered the first year of life, pneumonia being first, followed by diphtheria, tuberculosis, diarrhea, and measles. It was second in the age group 10-20 years, preceded only by tuberculosis, and third between the ages 20-40 years, tuberculosis being first and pneumonia second. After the 40th year, heart disease held first place.

Of the 34,597 deaths from heart disease, 41.1 per cent occurred after the 70th year, 50.6 per cent between the ages of 40 and 70, and only 8.3 per cent of the deaths were among persons under 40 years of age.

The curve of mortality from the beginning of the century has had an almost continuous rise from a rate of 133.5 in 1900 to 297.9 in 1928. There were only five recessions in this twenty-nine year period, the greatest of which occurred in 1919, when, as a sequel of the influenza epidemic the contingent of sufferers from impairments of the heart was considerably reduced. There is no unanimity among physicians and statisticians regarding the significance of this increase. In fact, some of them believe that the increase is more apparent than real. They stress the fact that the population of this country has been growing older, both because of the control of certain important causes of death in infancy and childhood and the resulting increase in the contingent of older persons, and in recent years the reduction in the volume of immigration which had given us hitherto an abnormally large proportion of young people. The mortality from heart disease being confined largely to the older ages, with an increase in the proportion of persons in those ages, the death rate naturally rose. Then we are told that improvements in diagnosis and the more careful statements of the cause of death, which has practically eliminated the rubric "old age" and reduced considerably deaths from causes "unknown," have also contributed to an increase in the recorded total of deaths from heart disease.

Let us now consider briefly some statistical sources of error in the recorded rates. There is, first of all, the fact that the statistical procedure as outlined in the International List of Causes of Death is revised every ten years, thus affecting the comparability of the rates. Of greater importance is the generally employed method of selecting the

cause to which a death should be assigned when a doctor enters two or more causes on the certificate. In 1925, for example, in the State, outside of New York City, almost one-half of the death certificates showed more than one cause. The selection is, of necessity, guided by the rather arbitrary set of rulings of the *Manual of Joint Causes of Death.* These instructions are at times contrary to the opinion of the certifying physician. In order to determine to what extent the occasional disagreements between the opinion of the physician and the statistical procedure influence the recorded death rates from heart disease, we have examined the certificates which were filed with the State Department of Health in March, 1928, in which heart disease was shown either as the primary or secondary cause. The results are shown in Table I.

TABLE I

DEATHS FROM DISEASES OF THE HEART BY AGE—MARCH, 1928, NEW YORK STATE (EXCLUSIVE OF NEW YORK CITY)

AGE	EDITED ACCORDING TO INTERNATIONAL LIST OF CAUSES OF DEATH AS:		CERTIFIED BY PHYSICIAN AS:	
	PRIMARY	SECONDARY	PRIMARY	SECONDARY
All ages	1,551*	635	1,451	735
Under 5 years	14	24	16	22
5- 9 years	3	8	6	5
10-14 years	5	4	6	3
15-19 years	5	8	9	4
20-24 years	8	9	8	9
25-29 years	13	18	18	13
30-34 years	18	18	22	14
35-39 years	25	16	30	11
40-44 years	40	24	38	26
45-49 years	49	38	51	36
50-54 years	86	45	80	51
55-59 years	122	52	120	54
60-64 years	160	71	149	82
65-69 years	193	83	176	100
70-74 years	225	76	209	92
75-79 years	246	59	218	87
80-84 years	198	52	174	76
85-89 years	100	20	86	34
90-94 years	33	9	30	12
95 years and over	8	1	5	4

*Including 13 delayed certificates for deaths which occurred in February.

The number of certificates totalled 2,186. In 1,451 of these, the physicians entered heart disease as the primary cause while, when edited according to the *Manual,* cases of primary heart disease numbered 1,551—an excess of 100, or 6.9 per cent.

The recorded number of deaths under 40 years totalled 91, the corresponding number assigned by physicians being 115. In other words, if the statements of the physicians were taken in all cases the death rate under 40 in March, 1928, would have been greater than the re-

corded rate by 26 per cent. In the older ages the reverse was true. At 40-60 years the recorded rate was 2.8 per cent higher and in the group 60 years and over it was 11.1 per cent higher than the rate based on the totals of primary cases assigned by the physicians.

The figures illustrate the degree of error arising out of the statistical procedure governing the tabulation of deaths according to cause. Although, to be sure, they represent the experience of only one month, the disparity between the recorded figures and the entries of the physicians would generally hold true for any month.

When we say, therefore, that the death rate from heart disease in the State, outside of New York City, was 308.3 in 1928, this number by no means measures accurately the mortality from this cause in the sense in which the reading of a clinical thermometer measures a patient's temperature. The difference between the present death rate and the rate, say, in 1900 is a still less accurate measurement of the change in the mortality during the twenty-nine year period.

Should one, therefore, forego an analysis of mortality from this and from certain other causes because of the large error contained in the figures, as in fact an eminent pathologist wrote to me some time ago? The answer to this question is, clearly, *no*. We cannot sit idle and blissfully await the day when the entire truth will be disclosed to us. A death rate is in a sense a theory which is constantly being made more accurate by the greater accumulation of knowledge.

While we do not know the exact number of deaths in which heart disease is the deciding factor, we do know that it is large. In 1928 almost thirty-five thousand deaths in the State were assigned to heart disease as the primary cause. If we were to consider the certifications of physicians and assume the degree of discrepancy deduced from the March, 1928 figures, the number would be reduced by 7 per cent to about thirty-two thousand. Although it is impossible to make a correction for errors in diagnosis, the number gives us a true picture of the relative position of heart disease among causes of death.

The mortality in old age, after the 70th year when more than two-fifths of the deaths occur, cannot be reduced to any appreciable extent since most of it is merely the natural result of the wearing out of vital organs due to the mere process of living. It is the younger ages that should be the concern of the physician and public health worker. In 1928 the deaths of 2,867 persons under 40 years of age were ascribed to heart disease. This is a larger number than the deaths at all ages during that year from diphtheria (863), influenza (1,943), all puerperal causes (1,295), and almost equal to the mortality from diabetes (3,069). There were recorded 2,927 deaths from heart disease in the age group 40-50 years, 5,630 deaths at 50-60 years, and 8,944 at 60-70 years.

The question naturally arises—can the mortality from heart disease in the younger ages be reduced and by what means? No satisfactory

answer to this question can be made without definite knowledge of the prevalence of heart disease, of its etiology, the present methods of treatment, and their effect. Here, preventive and curative medicine could make the best use of adequate morbidity statistics if they were available.

Official health agencies do not require the reporting of heart disease, the State and city sanitary codes limiting their lists to those diseases which are likely to spread from individual to individual. In this day, when the immutability of even chemical elements is no longer an axiom, the rigid grouping of diseases into communicable and non-communicable seems to be altogether artificial. Broad considerations of public health necessarily lead one to inquire into all causes of ill health. The existing system of disease reporting gives us only a partial answer.

Several years ago it occurred to us that it might be possible to interest a sufficient number of physicians in a coöperative study of morbidity of the "non-communicable" type. Although this expectation was contrary to what is supposed to be the practical American's credo, that "you cannot get something for nothing," I have always been convinced that most of us have an urge to spend some of our time in doing what we feel is worth while and for which we can expect no compensation other than the approval of our inner selves and the possible approbation of our neighbors.

The plan for a year's survey of sickness in the rural part of the State (to which I shall refer henceforth as the "Rural Survey") was presented in the summer of 1925 to a gathering of physicians and later published in *Health News*, the official organ of the Department. The response was most gratifying; more than one hundred physicians in thirty-three counties consented to make weekly reports on forms furnished by the Department of the occurrence in their practices of certain non-reportable diseases. This survey was carried out during the year 1927.

Later, it was decided to attempt a similar but more intensive survey of a single county and Essex was chosen for this purpose. The second survey, in which twenty physicians participated, continued for fifty-two weeks, October 2, 1927-September 29, 1928.

Let me summarize briefly the results of these surveys, especially those bearing on the subject of this paper. The total number of cases reported in the Rural Survey* was 98,069. Cases of heart disease numbered 4,123. In terms of the population (which was estimated as one hundred thousand), this indicates that about 4 per cent were suffering from some form of heart disease.

*Sickness in Rural New York. J. V. DePorte, Journal of the American Medical Association, Vol. 92, pp. 522-528.

This proportion is undoubtedly somewhat of an exaggeration since the forms on which the reports were made do not give the names of patients and it is possible that some cases may have been reported by more than one physician. In rural districts, however, the practice of changing physicians is not common and the degree of error introduced by repetition could not be considerable.

There were also reported 6,038 cases of tonsillitis, 3,234 of arteriosclerosis, 2,240 of chronic arthritis, and 1,543 of acute rheumatic fever.

In the Essex Survey* the total number of cases reported was 19,179. The form employed differed somewhat from that used in the Rural Survey, a new rubric "diseases of the skin" being added; syphilis subdivided into acquired and congenital, and diseases of the heart (this at the suggestion of Dr. R. H. Halsey), into rheumatic, syphilitic, and "other forms." Cases of heart disease numbered 535, or 3.0 per cent of the estimated population (18,000).

There were also reported 976 cases of tonsillitis, 569 of arteriosclerosis, 305 of chronic arthritis, and 87 of acute rheumatic fever.

The difference in the percentages shown in the two surveys is due in some measure to the more favorable age composition of the population of Essex County. We must also mention the fact that the physicians in Essex County were instructed to report cases of sickness among residents of the County only.

The Essex Survey also showed the etiology of the reported cases of heart disease. Of the 535 cases, 9 were given as syphilitic, 121 as rheumatic, and the rest, 405, as other types; in percentages—1.7, 22.6, and 75.7 respectively.

It is interesting to compare the number of cases of heart disease with all reportable communicable diseases. In the Rural Survey the cases of the latter totalled 3,212 as compared with 4,123 of heart disease; the corresponding numbers in the Essex Survey were 312 and 535. Cases of heart disease in both surveys exceeded the cases of reportable communicable diseases by practically one-third. These figures demonstrate in a striking manner the importance of the heart-disease problem in the State.

THE PREVALENCE OF HEART DISEASE

If we were to apply the imperfect and incomplete findings of the two surveys to the population of the entire State, we might say that cases of heart disease in the general population numbered between three and four hundred thousand. Another way to arrive at an estimate of the number of cases would be by means of the ratio of cases to deaths. During the fifty-two weeks of the Essex Survey the participating physicians filed 59 death certificates on which heart disease was given

*Sickness in Essex County. J. V. DePorte, New York State Journal of Medicine, November 1, 1929.

as the primary cause, or an average of 9 cases to one death. Time did not permit us to ascertain the number of deaths reported by the physicians in the Rural Survey. Assuming that the death rate was identical with that for the entire rural territory of the State, we find 295 as the estimated number of deaths, or an average of 14 cases to one death. Multiplying the number of deaths from heart disease recorded in the entire State in 1928 by these two ratios we get 310,000 and 480,000 cases respectively. Taking into consideration the various assumptions and estimates, we can say with a reasonable degree of certainty that there are at present in the entire State about three hundred thousand cases of heart disease.

A PLAN FOR THE STUDY OF HEART DISEASE IN THE STATE

The concluding paragraph of our report on the Essex County Survey read as follows:

> "The two surveys directed by the State Department of Health were made possible, through the *voluntary* cooperation of one hundred and twenty-seven busy practising physicians. This fact, in my opinion, is of transcending significance. The spirit of altruistic scientific inquiry manifested by these physicians encourages a hope of further investigations which could not be carried out in laboratories or offices of official and private health agencies."

A study of heart disease as seen in his everyday activities by the practising physician would seem to be a most appropriate continuation of the surveys conducted by the State Health Department. A group of diseases which incapacitates, partially or wholly, about three hundred thousand persons in the State is certainly a matter that cannot be excluded from the field of legitimate public health activities by the mere fiat of our individualistic tradition.

In the words of Dr. Theobald Smith,* "Public health operations deal with mass phenomena and consequently must use statistics . . . . As long as disease exists the operations of preventive medicine must be founded on our knowledge of disease . . . . All human inquiries are narrow and partial . . . . We must be satisfied with piecemeal work in the hope that occasionally some synthesizing genius will appear who can put the collected fragments together in some form acceptable to us and which will serve as a fresh pattern for further endeavors."

Dr. Smith speaks from the point of view of laboratory research, but his remarks apply equally well to statistical studies, such as we have in mind. I am confident that there will be no difficulty in securing the interest of a sufficient number of physicians who will agree to report periodically certain important facts relating to heart disease in their practice. The State Department of Health would collate the data and make them public from time to time. Unlike our earlier surveys,

*The Influence of Research in Bringing Into Closer Relationship the Practice of Medicine and Public Health Activities. Am. J. Med. Sc., December, 1929.

this study need not be limited to any definite period and could be carried on continuously. Since the average number of cases of heart disease in a physician's practice is relatively small, it would be possible, without trespassing too much upon his time, to employ a fairly complete form which would give us certain facts about the etiology of each case, the age, sex, color, conjugal state, and other essential information relating to the patient.

I hope that the American Heart Association will coöperate with us in this undertaking, particularly during the formative period. The value of such a study is self-evident. It should enable us, among other things, to determine in the course of years the results of the various types of treatment employed and at the same time it would certainly be of definite educative value to the participating physicians themselves.

THE CARDIAC CLINICS OF NEW YORK; THEIR ORIGIN, AIMS AND ACCOMPLISHMENT*

EDWIN P. MAYNARD, M.D.
BROOKLYN, N. Y.

ONE of the great tragedies that has confronted all of us who have undertaken the care of hospital ward patients, has been the spectacle of the rapid breakdown of our adult cardiacs when they have left the wards and returned to their old environments. As we have seen them come back for readmission, sadly broken down, perhaps two or three weeks after we had restored them to compensation, we have been depressed by the gravity of the situation and the plight of these afflicted people who must somehow work to live.

Back in 1911 this picture of human suffering and economic waste stirred Dr. Hubert V. Guile and his associates at Bellevue Hospital in New York to form the first clinic or "class," as it was then called, for adult cardiac patients. The primary object was to provide after-care for cardiacs discharged from the hospital wards, to teach them their limitations, to guide them in industry, and in so doing, to prevent or postpone the next breakdown and subsequent hospital admission. The success of this pioneer effort is too well known to require description. Through the years it has served as a model and now under the leadership of Dr. John Wyckoff it stands as one of our ideal clinics.

By 1915 the growing importance of the problem of heart disease was beginning to be appreciated by a few discerning physicians and lay people, with the result that they formed themselves into the Association for the Prevention and Relief of Heart Disease. This organization began to attack the problem of heart disease from a much broader point of view than that of the clinic. Its objects were to gather information upon heart disease, to develop and apply measures to prevent heart disease, to seek and provide occupations suitable for patients with heart disease, to promote the establishment of special dispensary classes or clinics, to extend the opportunities for convalescent care and permanent institutional care, to encourage the establishment of associations with similar objects in other cities and to maintain a central office and clearing house.

The effort of the A.P.R.H. to promote the establishment of special dispensary classes for cardiac patients was very successful and soon twenty-six clinics were started. Through the efforts of the Executive Committee of the A.P.R.H. these clinics were organized into an association of cardiac clinics in 1917 under the chairmanship of Dr. Robert H.

*Read at the annual meeting of the American Heart Association, February 4, 1930.

Halsey; and in 1923 this association became the Committee on Cardiac Clinics of the Association for the Prevention and Relief of Heart Disease.

It would be tedious to follow the developmental history of this Committee on Cardiac Clinics up to the present time. Suffice it to say that this original Association of Cardiac Clinics is now the Committee on Cardiac Clinics of the New York Tuberculosis & Health Association.

This outline of the evolution of the Committee on Cardiac Clinics in New York City has been given to illustrate one way in which clinics in any city can be organized and can become part of a larger public health organization.

The trend of our times in business is toward mergers to overcome the waste of great numbers of smaller organizations all working for the same object. The same is or should be the trend in public health. The multiplicity of organizations in our large cities all striving for very similar purposes is appalling. Mergers in public health work offer a logical solution of the difficulty and the way the original Association of Cardiac Clinics has developed to its present position is a good illustration of how this unification of effort can be accomplished.

Now let us pass to the aims of an association of cardiac clinics and see how and in what measure they are accomplished. Because of lack of knowledge of associations in other cities, it will be necessary to speak of our own Committee on Cardiac Clinics of the New York Tuberculosis & Health Association. Perhaps the first and predominating aim was to maintain and improve the standard of work done in the member clinics. Before this could be undertaken it was necessary to determine just what those standards should be, both for minimum requirements and for an ideal clinic. This was done in 1923 and the result published in a leaflet for distribution to the member clinics. By this step the committee provided itself with a measure by which it could not only judge the work of its member clinics, but establish admission requirements for new clinics.

The Executive Committee of the Committee on Cardiac Clinics was then provided with a secretary whose main duty is to visit member clinics, explain the organization and its aims to them, assist them in every way possible and report back to the Committee the status of each member clinic. In most instances the way in which improvements are initiated is by the suggestion of the secretary to the social worker or clinic chief at the time of the visit. The clinics usually respond to the best of their ability. However, if they do not, the executive committee studies the situation with great care and then makes a written recommendation to the clinic chief, to the hospital superintendent or to both. If these measures fail and the standard of work in the clinic remains below the minimum requirements for membership in the Committee on Cardiac Clinics, the board of trustees of the hospital is ad-

vised of the situation. If they fail to act, the clinic is dropped from membership. Fortunately this drastic step has been necessary in only one instance during the life of the organization. Thus a great deal of the time of the secretary and of the Executive Committee is devoted to the study of actual conditions in clinics and of methods of improving them.

One of the great difficulties in coördination of any sort of medical work lies in the lack of uniformity in terminology. The descriptions of the same disease or set of phenomena vary greatly. A group of workers in one clinic may speak of the functional capacity of a patient for instance, using terms that would mean very little to a group in another clinic. Early in its history, the Association of Cardiac Clinics recognized this and in 1921 adopted a system of functional diagnosis and classification based upon functional capacity as gauged by the patient's ability to carry on ordinary physical activity. This classification has been modified only slightly since its adoption and is familiar to you all. It has been of inestimable value in giving us a common standard or measure by means of which we can convey ideas to each other about the functional capacity of our patients. Its use is rigidly required, especially in applying for admission to convalescent homes.

In the matter of records of cardiac patients, the Association soon discovered that there was no uniformity whatsoever. Each member clinic had its own method and the amount and quality of the data recorded depended upon the interest of the physician in the clinic. The records were in no sense comparable. By 1923 record forms for history, physical examination and follow-up notes had been devised, which after much deliberation were adopted by the Association. These forms are now in use in twenty-seven clinics.

Aside from their great value in improving the records in the clinics and for statistical research, they have developed into a useful instrument in the hands of the Executive Committee of the Committee on Cardiac Clinics. This has come about in an interesting way. The Research Committee of the Heart Committee issues these charts to the clinics that desire them. At first they are issued in single sheets for which the clinics pay a moderate charge. The statistical workers of the Research Committee check up the quality of these records and after they are satisfied of their accuracy, they recommend to the Research Committee that these charts be issued to the approved clinics in duplicate and free of charge. At stated times the duplicate pages are torn off and collected for study by the Research Committee. At the same time these approved clinics are offered the assistance of statisticians from the Research Committee who work in the clinics during clinic hours helping the physicians with the records.

Very close coöperation exists between the Research Committee and the Committee on Cardiac Clinics. As was stated before, the main

interest of the latter is to maintain and improve the quality of work done in the member clinics. Through the studies of the Research Committee, the Committee on Cardiac Clinics can readily learn the quality of the records and therefore of the work done in the clinics that use the uniform charts. Good records and good work go hand in hand. When the records from a given clinic show persistent inaccuracies it is of vital interest to the Committee on Cardiac Clinics to remedy the situation. This it undertakes, usually by personal interviews between one of its own members and the chief of the clinic concerned. The Committee had found this phase of its work one of great delicacy and feels that it should not be entrusted to a lay worker. When properly approached, the response of the physicians in the clinics has been, with few exceptions, satisfactory. When the uniform charts were first devised they were looked upon purely as devices for statistical research. Now we have come to realize that they are one of the best means by which the medical work in the clinics can be evaluated and improved.

In another matter of uniformity, the Committee on Cardiac Clinics is indebted to the Criteria Committee. After years of effort, originating in the old Association of Cardiac Clinics in 1923, a nomenclature for heart disease has been devised and with it a set of criteria for use in connection with the nomenclature. This material is now published in a small book by the American Heart Association. It marks a great step in the progress toward a common language in the Cardiac Clinics.

Our executive secretary had not been long in the field when it became apparent that the clinic chiefs and social workers had no idea of the number of patients in their clinics, how many were active in attendance and how many were lost. Furthermore, they had little knowledge of the efficacy of their social service follow-up. The clinic chief did not know whether his clinic was growing and healthy or declining and encumbered with deadwood. Furthermore, the Committee on Cardiac Clinics had no idea of the heart situation as a whole in the city as expressed by the volume of work done in all the clinics.

To remedy this situation, a system of clinic bookkeeping was introduced and also a monthly report form modelled after the one in use in the tuberculosis clinics. At first, great difficulty was encountered in getting the clinic bookkeeping in such shape as to yield the data for the report, but after much effort by statisticians and social workers, the system was inaugurated. By the mere use of this form, the social worker and the clinic chief now have an accurate picture of the state of their clinic. They know how many active cases they are carrying, how many were discharged and the reasons, how many died and in how many the follow-up was unsuccessful. Furthermore, the Committee on Cardiac Clinics tabulates these reports in such a way that a fairly complete picture of the work done in the clinics is available each year.

In 1929 the Committee on Cardiac Clinics with the help of Dr. Philip S. Platt made a statistical analysis of the figures for 1928. It was realized at the outset that since this was the first year that many of the clinics were reporting, there would be many unavoidable statistical

Committee on Cardiac Clinics of Heart Committee

New York Tuberculosis and Health Association

244 MADISON AVENUE, NEW YORK CITY

Report of Children's / Adults' Cardiac Clinic of ________ Hospital For Month of ________ 192__

	ADULTS (16 YEARS AND OVER)	CHILDREN (UNDER 16 YEARS)	TOTAL
I. Composition of Case Load :			
1. Old Cases Brought Forward			
2. New Admissions			
3. Readmissions			
4. TOTAL			
II. Disposition of Case Load:			
A. Closed (Discharged, Transferred or Dropped)			
5. Diagnosed Cases of Organic Heart Disease (Class I, II, III)			
6. Abnormal Signs and Symptoms (Class E)			
7. Potential Heart Disease (Class F)			
8. Non-Cardiac (Other than Classes E and F)			
9. TOTAL			
B. Open (Balance to be Brought Forward Next Month)			
10. Diagnosed Cases of Organic Heart Disease (Class I, II, III)			
11. Abnormal Signs and Symptoms (Class E)			
12. Potential Heart Disease (Class F)			
13. TOTAL (10 + 11 + 12; also 4 — 9)			

DISPOSITION OF CLOSED CASES (Item 9)

Discharged:	Transferred:	Dropped:
14. Non-Cardiac	19. To Other Clinic or Institution	24. Not Found
15. Maximum Benefit Secured	20. To Other Dept. of Hospital	25. Follow-Up Unsuccessful
16. Clinic Treatment not advised	21. To Private Physician	
17. Died	22. Referred for Opinion Only	
18. Total	23. Total	26. Total

27. TOTAL CLOSED (18+23+26)________

COMPARATIVE CONDITION OF CLOSED CASES (Item 9)

28. Etiological Type:

Congenital	
Rheumatic	
Syphilitic	
Arterio-Sclerotic	
Hypertensive	
Unknown	
Other	
Multiple	
None (Non-Cardiac)	
Total	

29. Functional Capacity:

On Admission (A) Class	Total	On Discharge (B) Class I	II A	II B	III	E	F	Non-Cardiac*
I								
II A								
II B								
III								
E								
F								
Non-Cardiac*								
Total								

30. Clinic:
Number of Clinic Sessions during month ____
Total Clinic Hours during month ____
Total Clinic Visits during month ____

31. Personnel:

	NUMBER ON STAFF	TOTAL HOURS OF SERVICE DURING MONTH
Physicians		
Nurses		
Social Workers		
Volunteers		
Clerks		

32. Social Service Visits:
Number Routine Follow-Up Visits ____
Number Social Case Work Visits ____
TOTAL ____

33. Changes in Clinic Hours, Sessions or Staff:

Signed________ (Medical Social Worker)

*Other than Classes E and F

FORM 7-2M-2-29

SEE REVERSE SIDE

Fig. 1.

inaccuracies in the compilation. Nevertheless it was thought worth while to make a beginning and eighteen graphic charts were drawn comparing the forty-two clinics in many important points.

Figure 1 shows the monthly report form which is filled in by the

social worker in each clinic every month. Using data derived from these reports the graphic analysis of various phases of the work in the clinics in 1928 were made.

Figure 2 is a study of the percentage of new admissions per year. The clinics had been reporting regularly only for a short time before

Clinic Key No.	Total Case Load	New Admissions No.	New Admissions %
1....	122	87	71.3
2....	260	185	71.2
3....	188	128	68.1
4....	278	161	57.9
5....	110	63	57.3
6....	312	146	56.8
7....	331	170	51.4
8....	679	320	47.1
9....	238	112	47.1
10....	456	215	47.1
11....	219	103	47.0
12....	73	31	42.5
13....	90	38	42.2
14....	144	60	41.7
15....	153	63	41.2
16....	144	59	41.0
17....	254	95	37.4
18....	224	83	37.1
19....	380	138	36.3
20....	557	191	34.3
21....	367	126	34.3
22....	265	89	33.6
23....	473	157	33.2
24....	458	146	31.9
25....	161	51	31.7
26....	640	183	28.6
27....	215	61	28.4
28....	184	51	27.7
29....	184	48	26.1
30....	81	21	25.9
31....	196	50	25.5
32....	191	44	23.0
33....	382	88	23.0
34....	365	80	21.9
35....	108	23	21.3
36....	211	44	20.9
37....	527	109	20.7
38....	413	82	19.9
39....	305	58	19.0
40....	253	45	17.8
41....	492	85	17.3
42....	150	21	14.0

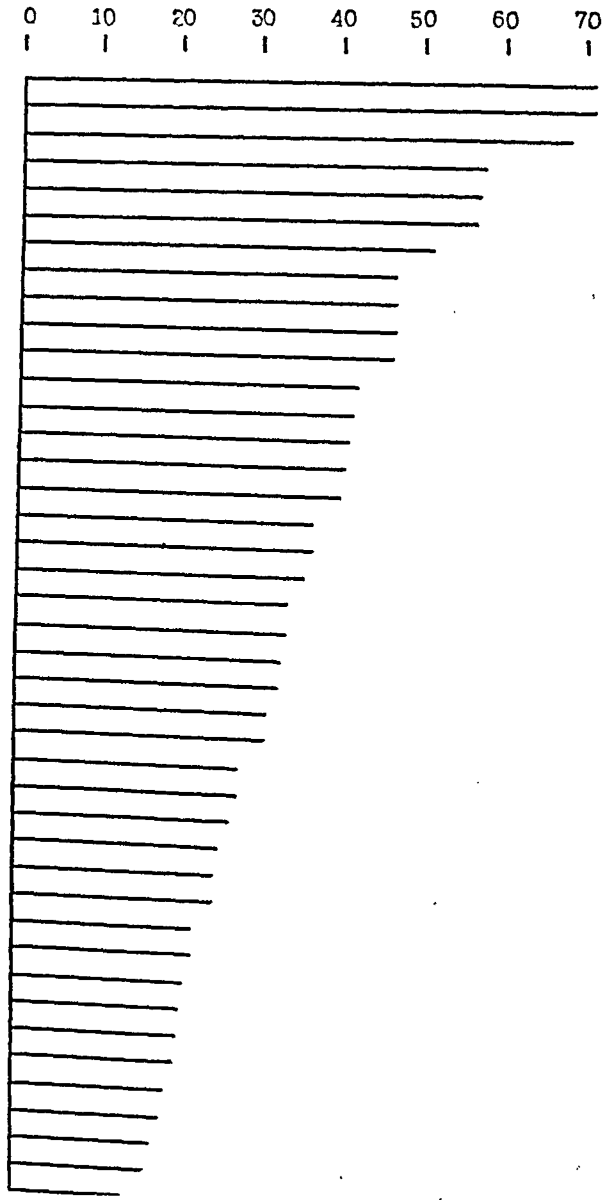

Fig. 2.

1928, and because of this, many statistical inaccuracies are undoubtedly present in the first year's work. For this reason the clinics have been listed by arbitrary numbers. A study of Figure 2 shows that there is a great variation in the growth of the individual clinics. Some are new and therefore show a high percentage of new cases and others do not appear to be growing at all.

In order to learn what was the average clinic practice and to throw some light on the efficiency of follow-up work in the clinics, similar tables were constructed to show the number of clinic visits per patient per year and the number of patients dropped per year. It does not necessarily follow that clinics with the fewest patients dropped had the best record. Perhaps in those clinics the standards of attendance and coöperation were too low and cases were kept enrolled which should have been closed.

It cannot be emphasized too strongly that the graphic charts of 1928 were an experiment to try out the method. It is planned to make a similar study with the more accurate figures of 1929, in the hope that in the future some sort of statistical measuring rod can be devised to demonstrate what constitutes good clinic practice as regards the matters studied in the charts.

There is one more phase of the work of the Committee on Cardiac Clinics that should be mentioned under the heading, educational. The committee holds two scientific meetings a year to which all the physicians and social workers in the clinics are invited. The program of one of these meetings is devoted entirely to the presentation of papers based upon work done in the Cardiac Clinics and to discussion of clinic problems. The other is of wider scope and speakers are usually invited from other cities to bring a fresh point of view to our clinics. The educational idea is carried still farther in that courses are arranged from time to time for social workers.

Enough has been said to make it obvious that the work of the Executive Committee of the Committee on Cardiac Clinics is both varied and interesting. In the constant effort to keep up and improve the standards in our clinics many difficult and delicate problems arise which require patience and tactful handling. In some instances, the Committee has failed, but more often, thanks to the intelligent coöperation of our clinic physicians, it has succeeded. Its objectives are twofold, to provide better care for the individual patient, and to secure accurate data for statistical research. As we grow older in the work we come to realize more and more clearly that careful records in themselves result in better care for the patient.

Department of Clinical Reports

COMPLETE HEART-BLOCK OF SEVEN YEARS' DURATION IN A CHILD RESULTING FROM INJURY

T. Homer Coffen, M.D.
Portland, Ore.

HEART-BLOCK (auriculo-ventricular dissociation) in children is not common. In 1922 Rosenson[1] collected 36 cases of heart-block in infancy and childhood and reported an additional case in a girl of 11 years with congenital heart disease. In the collected cases etiological factors were: diphtheria, 16 cases; rheumatism 2; congenital syphilis 1; cardiac tumor 1; nose and throat infection 1; associated congenital heart lesion 12; unknown 3. Heart-block occurring during diphtheria presents the gravest outlook, the mortality being 93.7 per cent in the collected cases.

Ernst Lorenz[2] in 1927 reported a case of functional partial heart-block. Romberg and White,[3] McIntosh[4] and Le Conte[5] reported heart-block in young children, probably of congenital origin and Sands[6] reported a case of a child of 6 years with three distinct attacks, one after scarlatina, one after diarrhea, with recovery after a few days. After nine months the block was still present.

Rosenson[1] reported the case of a boy of 10½ years who had heart-block resulting from a blow on the precordium. At this time Rosenson said this was the *only* case thus far reported with this etiology.

Morris Kahn and Samuel Kahn[7] in an admirable review of cardiovascular lesions following injury to the chest point out the variety of changes in rhythm and function resulting from injury from blows on the chest. "The superficial position of the heart and precordium exposes them to danger from injuries to the anterior chest wall. The character of the effects depends upon the status of the heart cycle at the moment of the accident, the resilience and resistance of the chest wall and the force, momentum and direction of the injuring force." They report auricular fibrillation, injury to valves, precordium, or rupture of the heart from chest injuries.

REPORT OF CASE

Kenneth K., now 10 years, fell from a wood pile four or five feet high when 3 years old (1922). The mother says that in trying to catch himself he hurt or fell

on the chest. He came into the house crying and complaining of pain in the upper abdomen. The mother did not see the fall; no bruises or wounds were seen. There was no cyanosis nor dyspnea. The child was in pain all night. The mother found the pulse rate 65 in the morning and took the child to the nearest town (18 miles distant), where it was found that the pulse rate was then 50. A diagnosis of intestinal obstruction was made and the child operated upon, but no obstruction was found. His pulse rate dropped to 36 and his condition was critical for a few days. In the next three months there was gradual improvement and he has been well since. His mother has been engaged in child welfare work and is certain that his pulse had always been normal. The child never had scarlet fever, diphtheria or other illness. Just before the accident he scored 98 per cent in a baby clinic examination.

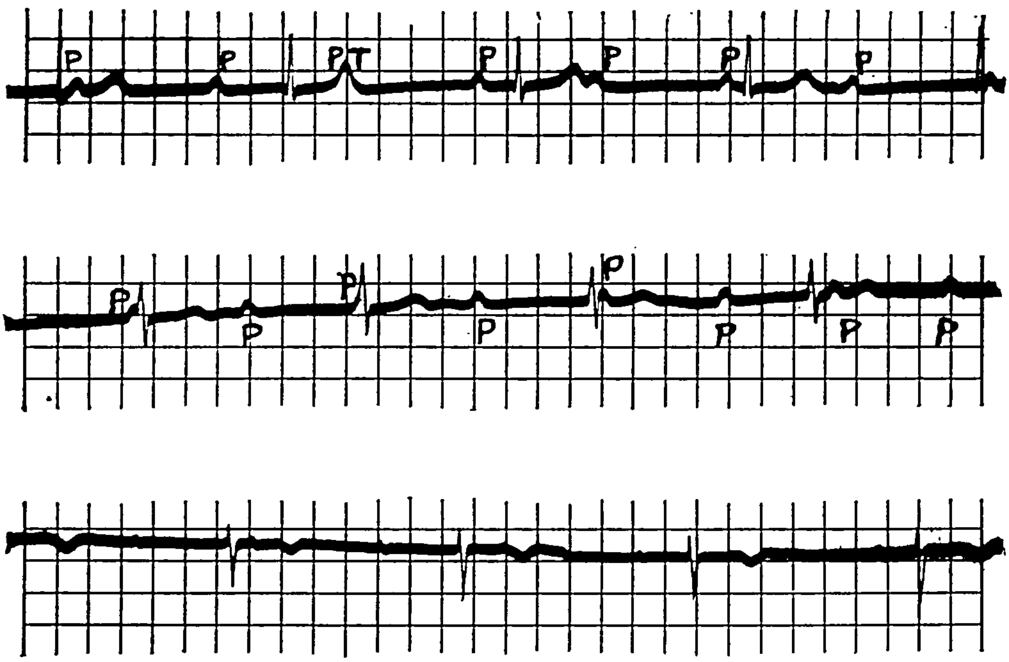

Fig. 1.

Examination: The boy was healthy in appearance, height 4′ 7¾″, weight 70½ lbs., color good, no cyanosis, pallor or abnormal pulsations in precordium or superficial vessels. The pulse was 48, regular. Eyes, ears, nose and throat negative. There was no adenopathy. The thyroid was not enlarged. The chest was symmetrical and negative. The heart borders were within normal limits though there was some increase in dulness in the waist. There was a systolic murmur at the pulmonic area, louder in the recumbent position. There was also a faint systolic murmur at the apex. In the recumbent position there was a positive wave suggesting auricular contractions about 80 per minute while the pulse rate was 48 per minute. The blood pressure was 90-95/80. The abdomen was negative, the liver not felt. There was no clubbing of fingers. The reflexes were normal. Urine and blood examinations were normal. Electrocardiograms show complete auriculo-ventricular dissociation, the auricular rate being about 80 while the ventricular rate is about

50. The P-complexes show no time relation to RT. The latter are normal (see Fig. 1). An orthodiagram (see Fig. 2) shows the globular type of heart with dulness in the waist (region of left auricle). In the right anterior oblique view the retrocardiac space was narrow but no abnormal notching of the esophagus was noted when barium was swallowed. In the left anterior oblique the left ventricle overrode the spine by about ½ inch. There were no abnormalities about the aorta or pulmonic area. There was no enlargement of the thymus or thyroid.

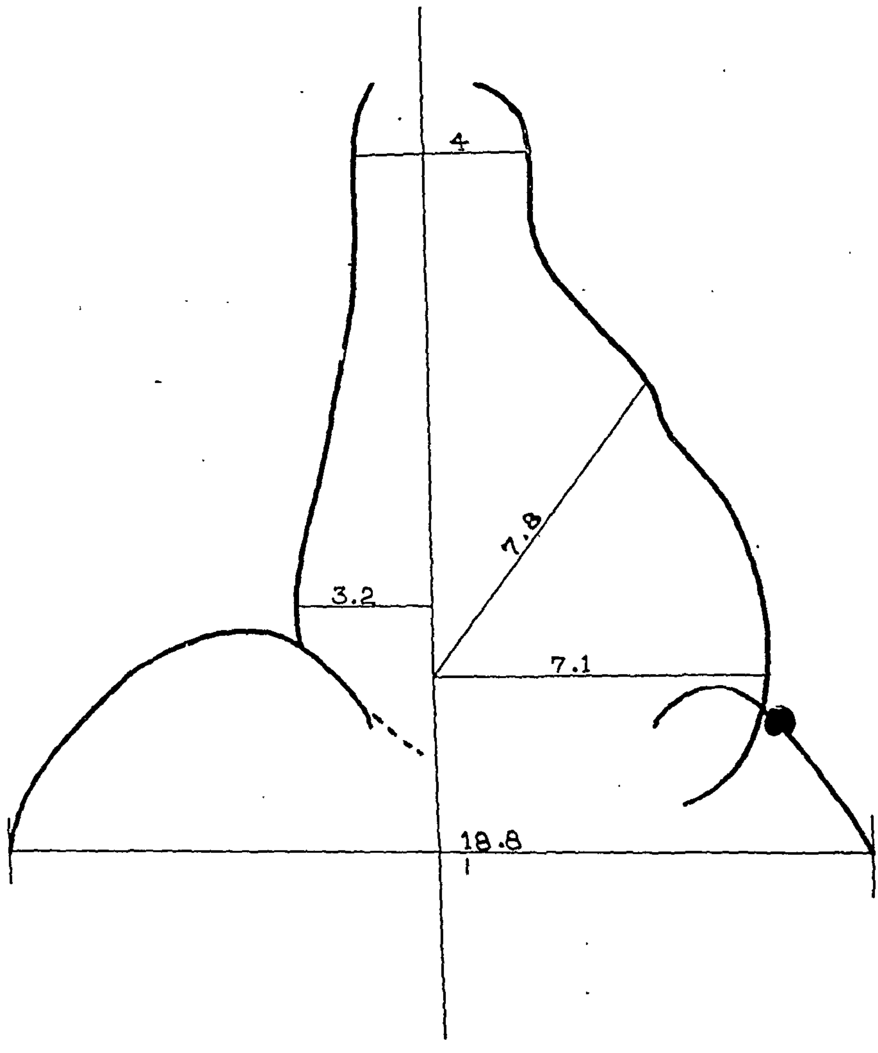

Fig. 2.—Kenneth K. April 20, 1929. Lungs: Entirely negative. Heart: Globular type but with very full waist. In the 1st oblique the space is narrow but no abnormal notching noted with barium. In the 2nd oblique the left ventricle overrides the spine ½ inch and on deep inspiration just failed to clear. The aortic window is clear.—E. L. B.

SUMMARY

A case of complete auriculo-ventricular dissociation is presented, occurring in a healthy appearing and physically active boy 10 years of age. It is presumed that an injury, sustained seven years before produced this condition, for he was a healthy child at the time of the accident. The pulse rate was very slow afterward and has remained so.

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INSULIN SHOCK AS THE CAUSE OF CARDIAC PAIN*

Case Report

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New York, N. Y.

THE symptoms of hypoglycemic shock respond promptly to the administration of glucose and usually cause little concern on a diabetic service. In fact, many clinicians believe that all diabetic patients who require insulin should be made to have at least one "shock" before leaving the hospital in order that they may become familiar with the premonitory symptoms of this condition. That this practice is not free from danger, particularly in patients with arteriosclerosis, is suggested by the following case report:

The patient was a fifty-eight-year-old Italian housewife. She was first seen in the Metabolism Clinic in February, 1923, when she stated that she had had diabetes for four years. She was advised as to her diet and did well until January, 1925, when an infection lowered her tolerance for sugar so that she was forced to enter the hospital for dietary regulation. She remained in the hospital for two weeks, became sugar-free, and was discharged without insulin. At the time of this first admission, cardiac symptoms and signs were not impressive. She stated that for several years she had had slight dyspnea and palpitation on exertion and also an "occasional feeling of distress over the left chest." The history is not exact, but it is clear that the patient was not greatly disturbed by these symptoms. On physical examination the heart did not seem enlarged, the sounds were of good quality and regular and there were no murmurs. The blood pressure was 155/90 mm. The radial arteries were firm. There were no electrocardiograms or x-ray studies at this time.

After discharge she remained under observation in the Metabolism Clinic until June, 1928, when it was decided that she should have insulin, and she was readmitted to the hospital. At that time she denied any cardiac symptoms. An x-ray film of the heart showed considerable enlargement, especially to the left. Calcification was apparent in the aortic arch. Her blood pressure was 135/85 mm. The electrocardiogram was essentially negative. The blood Wassermann was negative. She was not anemic.

On June 8, during the evening, she had an insulin shock. She became pale, covered with perspiration, nervous, and had a marked tachycardia. During this, she had an attack of severe precordial and substernal pain that radiated down the inner border of the left arm and into the left little finger. This pain was relieved promptly by amyl nitrite. A similar attack, under similar circumstances, occurred on June 22, and another on June 26. She was discharged again to the Metabolism Clinic and followed there. She had no more insulin shocks and no more anginal pain.

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In this elderly woman with an enlarged heart, it is interesting that the first insulin shock with its attendant tachycardia promptly produced a severe seizure of cardiac pain that twice recurred under similar circumstances. This clearly indicates the necessity for proceeding cautiously with the administration of insulin in diabetics who may have coronary sclerosis, lest unfortunate consequences result from insulin shock.

Department of Reviews and Abstracts

Selected Abstracts

Rösler, Hugo: On Congenital Isolated Dextrocardia. Wien. Arch. f. inn. Med. 19: 505, 1930.

This paper contains a very extensive and complete discussion on the subject based upon a thorough search of the literature from which the author has collected 38 cases verified by autopsy and 126 cases not so verified, but the author stresses the importance of anatomical verification, because otherwise partial situs inversus cannot be excluded.

The author describes his own seven cases. In the first case there was an *isolated* inversion of the ventricles and the large trunks as well as a transposition of the aorta alone into the right ventricle. The second case was remarkably free from symptoms, the third had peripheral malformations. On x-ray three cases had high dextroposition, twice there was a mirror-position of the heart, five times *atypical* shape of the cardiac shadow. In five cases the left diaphragm was higher than the right. One electrocardiogram was normal, one was diverted, one completely atypical, two had negative T-waves.

The 38 cases verified by autopsy are described and interpreted. The average age was eleven years, and various cardiac malformations were frequent and there were cases with situs solitus (the heart alone being transposed) combined with normal or transposed *origin* of the great vessels. The isolated congenital *dextrocardia* is not a malformation sui *generis*. No case is known with transposition of all parts of the heart and no case is known in which the heart and the great vessels were not malformed.

In the 126 cases described clinically the average age was 23½ years. Great exercise tolerance was noted *in many* of these cases. In many there were other malformations, especially defects in the muscles to the ribs. The apex beat was well demarcated, diffuse or even impalpable. Seventy-five cases had x-ray photographs, some had *mirror* pictures, others had atypical shadows. In the mirror forms the high dextroposition of the aorta predominates, in the atypical shadow forms the normal leftsided position. In most cases the right diaphragm was low, this difference between the diaphragms being caused by the cardiac position and not by the liver.

Twenty-nine electrocardiograms were obtained, 8 were normal, others had negative T-waves, with or without axis deviation. In these cases T-wave abnormalities had no prognostic significance. Q-waves were frequent, probably due to malposition. Disturbances of rhythm were rare. When the x-ray showed mirror picture, the electrocardiogram was usually inverted, the atypical x-rays (not "mirrored") would show positive electrocardiograms. The electrocardiographic interpretation was difficult on account of lack of material for verification, the anatomical relations being so very complicated and even the conduction system might be abnormal.

In a few cases it is possible for the patients to obtain a high age without impairment of cardiac function, but as a rule the prognosis is gloomy. About 350 references to the literature are appended.

Baker, Benjamin M.: The Effect of Cardiac Rate and the Inhalation of Oxygen on Transient Bundle-Branch Block. Arch. Int. Med. 45: 814, 1930.

It is the purpose of this communication to record further observations on temporary bundle-branch block and to discuss the nature of transient disturbances in the conduction of the excitatory process within the ventricular specialized tissue. A case report is made of a patient who showed signs of transient abnormal ventricular conduction whenever the period of rest between ventricular systoles was of sufficient length. The electrocardiograms showed that the intraventricular conduction time was within normal limits and whenever this period was somewhat shortened, faulty conduction ensued. Rest in bed and the administration of appropriate doses of digitalis afforded means of slowing the ventricular rate. It was also noted that the aberrant complexes disappeared during inhalation of oxygen. Also during the administration of oxygen although the cardiac rate was increased by exercise well above the point provoking delayed conduction in all previous observations the normal appearance of the ventricular complexes was retained.

Dressler, Wilhelm: On the Formation of Interference, Dissociation and of Retrograde Propagation of Ventricular Extrasystoles. Wien. Arch. f. inn. Med. 19: 611, 1930.

The authors have studied cases where a disturbance of impulse formation has led to a permanent nodal rhythm.

Report follows of a case with nodal rhythm, where for some reason the complexes discontinue to travel backward to the auricle. Then impulses originate in the sinus node and with delayed conduction time travel to the ventricle where they produce complexes which have a tendency to become atypical. This change from nodal to auricular rhythm occurred abruptly. Changes in shapes of P-waves suggest various places of origin for auricular contractions; such interchange of various centres of origin is not uncommon where the superior centre is depressed, especially as a vagus effect. The patient also showed ventricular extrasystoles which were followed by a wave strongly suggesting a P-wave—probably these are retrograde extrasystoles. These must be considered a rare occurrence.

Another patient had sinus depression, lasting as long as 3.5 seconds if he held his breath; during this period escaped beats or nodal rhythm would occur, this would occasionally be interrupted by complexes which the authors thought originated high in the A-V node. Some years later this gave place to a definite nodal rhythm.

These observations led the authors to this problem: Why, in some cases, does nodal rhythm fail to produce auricular contractions? Authors produce evidence that the nodal impulses do not even travel back toward the auricle, the retrograde conductivity being so difficult as to prevent some of the nodal impulses from traveling backward. In such cases where nodal rhythm is regularly associated with auricular contractions, the conduction system has been trained to retrograde conduction; this is supported by the frequent occurrence of auricular complexes after extrasystoles occurring in nodal rhythm.

Vagus effect might cause the rhythm to change from nodal to "interferenzdissoziation," and sympathetic stimulation would cause the reverse change.

Dressler, Wilhelm: Disturbed Conduction in the Auricle. Med. Klin. 25: 185, 1929.

Lewis wrote in 1925: "So far as we know, 'aberration' is peculiar to the ventricle, the auricle is exempt, because in its structure it possesses no special conduction paths."

Scherf and Shookhoff produced nodal rhythm in dogs; when the nodal rhythm was resumed after extrasystoles, the nodal extrasystoles were associated with changes in P-waves. These might even become positive. This is explained by the impulses using different pathways through the auricle. Rothberger and Scherf ligated the upper and lower end of the sinus node and obtained a sinus rhythm with negative P-waves. They thought this was due to atypical conduction paths, for ligation along the sides of the sinus node produced no change in P-waves. Therefore, P-waves of atypical auricular activation may be positive and of sinus rhythm may be negative, all depending upon the journey of the impulse through the auricle.

Two case reports follow: One patient had auricular extrasystoles preceded by an upright but atypical P-wave and shortened P-R interval. This shortened P-R interval causes the author to diagnose nodal extrasystole originating high in the node and with positive P-wave, and on the basis of the experimental evidence quoted above, ascribes the form of the P-wave to the atypical retrograde course of the impulse, finding the usual path refractory. He emphasizes the rarity of such a finding. As a rule in nodal rhythm P is positive when it precedes the R, negative when it follows. The author argues against the interpretation of wandering pacemaker in cases of nodal rhythm where the P-R interval changes as well as the shape of the P-wave. A critical discussion on other reported cases follows.

Another patient had partial block, some auricular impulses being entirely blocked, the P-waves following such pauses all had atypical shapes. The atypical P-waves had presumably the same origin as the regular ones, the timing being absolutely regular. Therefore the atypical shape must be due to an atypical course. To the author's knowledge this is the only case on record where P-waves changed shape under these circumstances. Moenckeberg has shown that pathological processes in the auricular myocardium may cause partial or complete heart-block. This may be the explanation in this second case.

Dressler, Wilhelm: Dissociation and Interference in Partial Heart-Block. Ztschr. f. klin. Med. **111**: 23, 1929.

In pararhythmias two centers of unequal frequency are active, the slower being protected by blocking from the other. Occasionally equal frequency of both centers may lead to a dissociated function of auricle and ventricle; this state in the course of change of one rhythm to another has wrongly been termed wandering of the pacemaker in the A-V node. Author reports a case with two pacemakers of equal frequency, and on the basis thereof discusses the conditions under which both centers become active.

A case of bradycardia (44 beats per minute) showed an electrocardiogram with ventricular complexes at even intervals, while the interval between the P-waves was constantly changing. The change in auricular intervals did not influence the P-R intervals. There the authors were not dealing with partial heart-block, but with automatic ventricular rhythm, the impulses of which did not affect the auricular rhythm, because they found the auricles refractory from the preceding auricular contractions. This case makes the author ask: Under which conditions will two centers of equal frequency produce a dissociation of two cardiac sections? That can only be done when the two centers beat quite or almost synchronously. If impulses originate in one focus too early the impulses will cause a contraction of the entire heart, preventing further ectopic impulse formation.

Another case showed complete heart-block with double rhythm, two auriculo-ventricular to one automatic ventricular contraction. Sometimes an auricular systole occurred, when a refractory period of the ventricle had passed off and before the

next ventricular contraction; in this case the impulse was conducted through and resulted in a ventricular contraction.

The two factors which determine the disturbance of rhythm are frequency of the impulses and the duration of refractory period. But the refractory period varies from beat to beat, but in all cases does it exceed the sinus-interval, for otherwise sinus rhythm would be established; it is shorter than twice the sinus-interval, for if it approaches or exceeds, the auricle again determines the cardiac contractions (2:1 heart-block), or the same condition occurs as in case 1.

Extrasystoles would prevent transmission of auricular impulses, which according to the time of their occurrence ought to have been transmitted, thus showing retrograde transmission of the impulses, sufficient to cause refractory blocking of the conduction path.

These cases make intelligible the complete A-V dissociation in ventricular tachycardia, because the ventricular intervals are shorter than the refractory period of *the conduction system plus the conduction time of another impulse.*

Another case showed a marked arrhythmia of the auricles, varying from .59 to .95 seconds. The ventricular complexes also had irregular intervals and fell into two groups, in one the interventricular intervals changed between .98 and .105, in the other between 1.23 and 1.26; long and short periods alternated, every other complex was automatic, *and every other one (the ones following the shorter periods)* was conducted down from above. So here was a 2:1 block interfering *with a regular ventricular rhythm.*

Such cases as these are rare in the literature. They are characterized by a combination of sinus rhythm and automatic ventricular action, the impulses of which are not conducted backwards. The refractory phase of the bundle is longer than at least one sinus interval, so that the automatic ventricular period is shorter than the interval between two effectively conducted auricular impulses. Only such auricular impulses are conducted to the ventricle as fall after the refractory period of the bundle, and disturb here, being premature, the regular ventricular rhythm. But if the automatic ventricular interval is shorter than refractory period plus conduction time, then complete dissociation occurs.

These arrhythmias are not caused by disturbances in conduction, but primarily by the occurrence of a second focus of impulse formation. This may be the cause of complete block more frequently than is generally supposed. Both from the point of view of prognosis and of treatment it is important to distinguish between complete heart-block and partial block with dissociation; the latter having a more favorable prognosis. Also a complete block with certain time relation may *mimic a 2:1 block.*

The authors finally give the following classification of these "pararhythmias"; *that is arrhythmias with two cardiac foci of impulses.*

1. Interferences: one focus dominates while another focus (the interfering one) manifests itself in the entire heart or a part thereof.
2. Total dissociation of auricle and ventricle.
   a With maintained conduction system.
   b With complete block.
3. *Dissociation with interference is a combination of 1 and of 2a.*

Fischer, Robert, and Kiss, Aristid: A Contribution to the Knowledge of Pararhythmia. Deutsches Arch. f. klin. Med. 164: 73, 1929.

The pararhythmia was observed in a patient with rheumatic heart disease, and with a P-R interval of 0.260 sec. to 0.280 sec. and automatic ventricular contractions, singular or in groups, which sometimes dominated the rhythm. The shape of these extrasystoles was definitely atypical. When sinus rhythm was established after a period of such extrasystoles, the P-R time was at first very must pro-

longed and became gradually shortened down to 0.280 sec. This is the opposite of what is seen in certain forms of heart-block (Wenckebach's periods). This variation in conduction time actually determined the onset and cessation of idioventricular rhythm. On account of the disturbance of conduction this was not considered dissociation with interference, in which never more than one normal beat at a time interrupts the idioventricular rhythm, which is of higher frequency. It is only because the A-V conduction time is constantly shortened that sinus beats continue to come through, though the sinus rhythm is shorter than the idioventricular rhythm. Probably this disturbance of conduction is also responsible for the failure of retroconduction of the extrasystoles. While the pararhythmia existed it was occasionally interfered with, because the P-P intervals were but very slightly longer than the P-R intervals.

Dressler, Wilhelm: Permanent Nodal Rhythm, With Attacks of Unconsciousness Caused by Ventricular Flutter. Klin. Wchnschr. 8: 165, 1929.

Case report. Male fifty-three years of age, complained of dyspnea and dizziness and lately also of attacks of unconsciousness, which were becoming more frequent. Nodal rhythm was present at a rate of 38 per minute. Probably the focus was low in the node. Sinus rhythm was occasionally present.

The attacks of unconsciousness were ushered in by a feeling of flutter over the precordium and they lasted two to three minutes. He also occasionally had attacks of "pulling" in the chest associated with dizziness. These light attacks were observed electrocardiographically: at first single and later massed heterogeneous extrasystoles occurred at a rate of 200 per minute; in certain series they were homogeneous and reminded the authors so much of auricular flutter, that they called them ventricular flutter. During these attacks the pulse was not felt.

The author believes coronary disease to be the etiological factor. The differential diagnosis is from Adams-Stokes' syndrome, particularly because both forms of attacks occur with heart-block, and is considered relatively important; the prognosis is more serious in flutter, and the drugs recommended in the treatment of Adams-Stokes' syndrome (strophanthin, adrenalin, barium chloride) are apt to aggravate flutter.

Geraudel, E.: The Sign of "Satellite Auricular Contraction" in Adams-Stokes' Syndrome. Arch. d. mal. du coeur. 23: 18, 1930.

As a result of previous work the author begins with the following conclusions: The right auricle anatomically consists of two parts, one originating from the sinus and one from the atrium. The sinus vestibule represents the most upper part of the cardiac tube. It is connected on one hand to the atrial cavity and on the other to the ventricular cavity.

Strictly speaking the ventricular cavities communicate with the sinus cavity not with the atrial cavity. This sino-ventricular communication consists of two parts, a lower corresponding to the bundle and a higher one. Therefore, Adams-Stokes' syndrome may occur due to interference with conduction high in the vestibule or lower in the bundle.

The author has also shown that electrocardiographically the negative P-wave is of special importance. This has hitherto been considered evidence of auricular contraction occurring from below upward (retrograde contraction), while the positive P-wave showed the contraction spreading from above downward. The author provisionally assumes that the ectopic auricular focus is placed in the subeustachian sinus of Keith. The sinus communicates with auricular and ventricular cavities through four muscle bundles: (1) one to the superior auricle, (2) one to the inferior auricle, (3) a second one to the inferior auricle, (4) one with the ven-

tricles. That is; the lower auricle is controlled by two bundles which later unite in a common trunk, one of which runs in the upper and one in the lower part of the auricle.

The normal auricular contraction is a combination of the activities of the upper and the lower centers, the latter being subordinate. Of the two bundles going from the lower center, one is the lower bundle to the lower auricle, another is the one to the ventricles. The evidence of activity of the lower center is included in the QRST complex, occurring during the iso-electric period between the S and T, and may be ignored.

If the waves from both auricular centers are superimposed, they may be difficult to differentiate.

The fact that the lower auricle is supplied both from an upper and a lower branch has important consequences. In the normal heart the impulse comes through the upper path and the contraction wave coincides with the upper auricle. *Pathologically* blocks *may occur in various places, for instance, a partial* block may occur in the lower bundle above the point where the bundle to the lower auricular center separates from the ventricular bundle. Then the lower auricle is controlled by the upper center; under certain circumstances, however, the partially blocked impulse traveling the lower path may find the lower center at a time when the refractory period following the upper impulse has passed off. Then results a lower auricular contraction coinciding with the ventricular contraction.

This coincidence of contraction of lower auricle and ventricle may also occur if the upper path to the lower auricle has been interfered with, so the lower auricular center is not rendered refractory by the impulse traveling the upper path.

The form of the P-wave has therefore a certain diagnostic value, determining the site and the extent of auricular block. One can determine whether Adams-Stokes' syndrome is due to block in the bundle of His or in the auricular pathways.

In view of this knowledge the author has reviewed 397 electrocardiograms from 49 patients with Adams-Stokes' syndrome.

Eleven had marked P-waves from the lower auricular center, in these therefore, the block is situated not in the bundle, but above the bundle. Records of these cases are given.

Henderson, Yandell, and Mobitz, Woldemar: The Constant Rate of Absorption of Ethyl Iodide Vapor and Its Significance as a Basis for Measuring the Circulation. Am. J. Physiol. 92: 707, 1930.

This article represents a reply to the criticisms that have been raised to the use of this method of estimating the blood flow. The authors deal particularly with: (1) Analysis by means of iodine pentoxide, (2) The automatic sampling of alveolar air, (3) The coefficient or effective coefficient determining the passage of ethyl iodide into the alveolar air into the lungs.

The method of analysis by means of iodine pentoxide when properly used is reliable and accurate as well *as simpler and more rapid than other methods.* All methods of analysis for calculating the circulation should be controlled by estimations of the dead space.

Automatic sampling of alveolar air is now established as a reliable technic.

During quiet breathing no considerable error is involved in using as true alveolar air the last portion of full normal expiration.

The authors then discuss the various factors to be considered in determining the passage of ethyl iodide from the alveolar air into the blood in the lungs. They believe that the method is satisfactory.

Ernstene, A. Carlton, and Blumgart, Herrman L.: Orthopnea. Its Relation to the Increased Venous Pressure of Myocardial Failure. Arch. Int. Med. 45: 593, 1930.

The authors believe that the orthopneic position benefits the patient with congestive circulatory failure because it secures a maximum blood flow about the respiratory center and thereby relieves the patient from the distress due to partial asphyxia in that area. Accordingly, a patient with myocardial failure and increased venous pressure always tends to maintain an elevation in bed sufficient to keep the respiratory center above the meniscus of the column of venous blood extending upward from the right auricle. In the upright position, pressure in the veins about the respiratory center is kept more nearly normal than in any other position and the blood flow in the capillaries feeding these veins is increased to the maximal limit set by the existing myocardial failure.

In order to test the validity of the hypothesis, 82 comparisons of the height of venous pressure and the degree of orthopnea were made in 22 patients with uncomplicated myocardial failure of the congestive type. A parallelism between the two measurements was observed. In general, it was found that the higher the venous pressure the greater was the orthopnea.

When *orthopneic* patients were placed in the recumbent position with the head flat, simple elevation of the head by flexion of it on the thorax produced, almost without exception, conspicuous diminution of respiratory distress. This procedure favors diminution of the cerebral venous pressure but has no significant effect on the vital capacity of the lungs.

Jolliffe, Norman: Liver Function in Congestive Heart Failure. J. Clin. Investigation. 8: 419, 1930.

The frequency of clinical jaundice in a series of 231 patients with congestive heart failure was observed to be 2.1 per cent. Fifteen of the sixteen patients had some *alteration in liver function though no characteristic type was found.*

No parallelism between the degree of heart failure and the impairment of liver function could be noted in individual cases. There was perhaps a parallelism between the changes in liver function and the degree of edema and size of the liver.

The author believes that liver *dysfunction* induced by an *attack* of chronic passive congestion is not permanent and that when it persists following recovery from passive congestion an independent liver impairment should be suspected.

Dock, W., and Tainter, M. L.: The Circulatory Changes After Full Therapeutic Doses of Digitalis, With a Critical Discussion of Views on Cardiac Output. J. Clin. Investigation. 8: 467, 1930.

A critical review is made of the older and current views of the actions of digitalis on the circulation and an attempt has been made by experiments on dogs to correlate its influence on the heart and peripheral vessels with diminution in cardiac output. The action of the drug in man varies with the functional state of the circulation in determining the output. When the normal heart is studied in animals and probably in man, there is a reduction following the use of digitalis but in such *pathological states as heart failure* with chronic passive congestion, digitalis would seem to tend to increase the cardiac output and to restore the venous pressure to a normal level.

Smith, W. Carter, Walker, George L., and Alt, Howard L.: The Cardiac Output in Heart Disease. Arch. Int. Med. 45: 706, 1930.

In this study the authors have observed the response of the circulation particularly as regards the output of the heart in several types of heart disease in-

cluding complete heart-block, auricular fibrillation before and after the restoration of normal rhythm, subacute rheumatic fever and chronic rheumatic valvular disease. None of these cases showed signs of congestive failure of the heart. The output of the heart was measured by the method of Field, Bock, Gildea and Lathrop.

The output of the heart was studied in three patients with complete block. The minute output of the heart was within the range of normal but each had a greatly increased stroke volume. Of the three patients with auricular fibrillation, the two with mitral stenosis showed an increase in cardiac output of one-fourth or more when the rhythm became regular. The cardiac output of one of these patients was the same with the irregularity of auricular fibrillation as with a regular sino-auricular rhythm caused by auricular premature contractions. When a regular rhythm without premature contractions was established there was a 29 per cent increase in the cardiac output. A third patient who had a pulse deficit of from 15 to 20 a minute but no mitral stenosis showed a corresponding increase in output when the pulse deficit was eliminated with digitalis. The patient with subacute rheumatic fever and with chronic rheumatic valvular disease associated with regular rhythm showed considerable fluctuation but was within normal limits.

With the onset of congestive failure of the heart there may be an increase in the output of the heart.

Deutsch, Felix: Variation in Heart Size, Especially the Diminishing Heart, Immediately After Exercise in Sports. Arbeitsphysiologie, 2: 215, 1929.

The changes which the heart undergoes after exercise are not yet conclusively investigated.

Author studied participants in the Olympic games.

There is evidence that sportsmen's hearts are larger during the season when they are in training than during the "dead season." In one case the cardiac diameter was increased 5.1 cm. above the calculated normal. After the intense exercise of the fight, the heart was barely larger than the calculated normal; that is, it diminished during the exercise. Within a few days it regained its former size.

The greatest diminution amounted to 3.2 cm.; that is, one-fifth of the original size. All except four hearts diminished in size.

The author discusses the causes of this change: the tachycardia, the diminished amount of circulating blood (much blood remaining in the periphery, and much fluid being lost during exercise) and others are considered.

The diminution of size lasts until recovery occurs.

Kahn, Morris H.: Auricular Flutter Following Direct Injury to the Chest. Am. J. M. Sc. 179: 605, 1930.

A case is reported in which following direct violence to the chest auricular flutter was discovered with signs of heart failure. The electrocardiographic records confirm the diagnosis. The patient died four months after the accident without post-mortem examination. The condition persisted in spite of treatment and was unimproved when last seen. The possibility of subepicardial ecchymosis in the auricular muscle is to be considered as the cause of the condition. It was noted in the electrocardiogram that the alternate ventricular cycles occur after every four and every two auricular contractions. In taking blood pressure measurements this produces an arrhythmia with the impression of a distinct pulsus alternans with a difference of 30 mm. in the systolic pressure between alternate cycles. This difference is equivalent to half the pulse pressure. The author surmises from this that the auricular function in this case was a most important one in producing

ventricular filling. Apparently every contraction of the auricle during flutter contributes its definite measure of blood to the ventricular volume.

It was also noted that preceding every ventricular cycle that follows two auricular contractions there is a normal P-R interval of 0.2 second. When four auricular waves occur, conduction becomes reduced to 0.14 second. It is thus seen that there is an improvement of conductivity following the longer periods of block.

Fordyce, A. Dingwall: Undetected Syphilis and Rheumatic Infection in Childhood. Brit. M. J. 1: 530, 1930.

This study describes the details of nine children with rheumatic heart disease who were also congenital syphilitics and in whom the striking feature was the absence of clinical signs pointing to the presence of a syphilitic infection. The author suggests that an important subgroup of rheumatic children can be defined in whom the rheumatic infection is superimposed upon congenital syphilitic infection and untreated, undetected syphilis.

Barr, Sir James: The Preservation of a Healthy and Efficient Circulatory System From Childhood to Advanced Age. Brit. M. J. 1: 769, 1930.

The author has interested himself in the physical side of the function of the heart and the peripheral circulation. He believes that through regulation of exercise and other influences, such as internal gland secretion, and elimination over long periods of years, that the circulation can be improved and altered. He stresses particularly abuse of the body from infection, alcohol, tobacco and exercise. The viewpoint expressed in this survey is extremely important and one which at times may be lost sight of.

Herpath, C. E. K., and Perry, C. B.: The Coronary Arteries in a Case of Familial Liability to Sudden Death. Brit. M. J. Apr. 12, 1930, p. 685.

This report supplements one made by Coombs and Lucas describing a family of whom the father and two sons had died with great suddenness. They had examined the heart of one of these sons, a man aged 32, who had been taken ill while playing football and had died within an hour or so. It was found to present macroscopical changes apparently of an atheromatous type in the coronary arteries.

The present report describes the findings in a third son who died suddenly. Electrocardiograms and the history and physical examination are given. Postmortem examination including radiograms of the injected heart specimens showed degenerative changes in the coronary artery. The authors describe the pathological process as one of premature senility of the arterial tree with a particular incidence on the coronary arteries.

Robey, William H., and Finland, Maxwell: Effect of Tonsillectomy on the Acute Attack of Rheumatic Fever. Arch. Int. Med. 45: 772, 1930.

The authors present briefly some of the results of their experiments with enucleating the tonsils during the acute attack of rheumatic fever. In a period of five years there were 165 patients included in the study. Of these, 71 were operated on during their residence in the Boston City Hospital for polyarthritis, leaving 94 as controls. Among the 71 operative cases, there was definite clinical evidence of activity at the time of the operation in 50; the remaining 21 cases were apparently quiescent. Some of the patients had previously been subjected to tonsillectomy but about one-half of these had remains of tonsillar tissue.

The authors believe that the earlier the focus of infection is discovered, the greater the possibility of removing it, thus lessening the recurrence of attack, the length of time in the hospital and the danger of cardiac involvement. The

removal of the focus can be performed as readily at the end of one week as four. They believe that tonsillectomy may be performed during the active stage of acute rheumatic fever without harm to the patient from the operation. Tonsillectomy at this time offers no more dangers than when performed under what appear to be the most favorable conditions. They state that tonsillectomy may produce an exacerbation of the joint symptoms but that it will probably be mild and brief if the operation is a success. This point should be explained to patients beforehand.

Cobe, Herbert Marshall: The Incidence of Bacteria in 400 Tonsil Cultures. J. Infect. Dis. 46: 298, 1930.

In 400 tonsillar cultures staphylococci were the predominating organism. Streptococci followed the pneumococci in predominance, with the hemolytic streptococci the predominant members of the group. Three per cent of the nonhemolytic streptococci recovered are classed as streptococcus cardioarthritidis. The nature of the disease which led the patient to have tonsillectomy is not stated.

From this study there appears to be a definite relationship between the type of organism recovered from tonsillar cultures and the age of the patient, streptococci being more common in younger patients. There also seems to be a definite seasonal difference in the organisms recovered from tonsillar cultures: B. influenzae, B. mucosuscapsulatus, and the diphtheroids all being more prevalent in the spring; Micrococcus catarrhalis more prevalent in the fall.

Lewis, Sir Thomas: Early Signs of Cardiac Failure of the Congestive Type. Brit. M. J. 1: 849, 1930.

The author believes that the question of the capacity of the heart for work is a most important one when a patient seeks advice and disease of the heart is suspected. The answer to this question should dominate both the prognosis and treatment. He discusses among the early signs of cardiac failure, breathlessness, increased venous congestion, visible and venous pulsation and enlargement of the liver.

The author believes that attempts to estimate cardiac output in terms of fluid volume, while important from a physiological standpoint have as yet found no application in clinical work and are unlikely to find such application for many years to come.

Breathlessness occurs as first main symptom of cardiac failure. This breathlessness should be measured not in terms of degree but in terms of effort which produces this symptom. When breathlessness is present, when the patient is at rest cardiac failure is well established and other symptoms make their appearance.

In order to measure venous pressure, the author employs the simple manometer connected to a wide needle with the blood within a vein. When the blood enters this manometer, the level at which it rests in comparison with the level of the manubrium sterni and the level of the right auricle indicates the degree of venous obstruction. It is possible to note the point at which peripheral veins especially in the neck and in the arm collapse when compared with the level of the manubrium sterni. This older method with certain restrictions is a most satisfactory method for estimating venous congestion.

The author also points out that the level at which the venous pulsation reaches its maximum intensity may be utilized as the level of venous pressure. The details of these observations are explained.

He describes the observations of venous pulsation in normal and in abnormal subjects with venous congestion. The veins can be seen to pulsate in the superficial veins of the neck, or can be felt over the larger and deeper vessels in the neck.

Enlargement of the liver occurs in a latter stage of venous congestion and is a valuable sign of cardiac failure.

Hift, Robert: On Treatment of Luetic Aortitis. Wien. klin. Wchnschr. 42: 33, 1929.

The importance of the serum reaction is emphasized. This may be negative in well-established cases. Also a positive reaction may occur in a resting infection.

Schottmüller's classification is given: supravalvular, valvular, coronary and aneurysmal lues. Luetic valvular disease or aneurysms do not alter the prognosis sufficiently to change the intensity of the treatment. The severity of the findings are not directly proportional to the intensity of the disease. It is more important to pay attention to the general health of the patients, and to interference with the circulation, hypertension, arteriosclerosis, etc. Subjective symptoms often count more than objective ones, and form the best indication of the progress of the treatment.

These are divided into symptoms from the central nervous system, pains (angina), cardiac neurosis, circulatory insufficiency, and symptoms due to aneurysms.

Only the pathological lesions which have not reached the stage of scar formation are susceptible to treatment. The clearing of active lesions may be preceded by flare-ups (Jarisch-Herxheimer reactions). This is probably a chemo-reaction of the tissues. It may be produced not only by salvarsan, but also by bismuth and mercury.

The author discusses the sudden death in this disease, and shows that it has nothing to do with the treatment, as it frequently occurs in cases not treated.

The duration of life from the onset of symptoms seems to be longer in patients who have been treated.

The Herxheimer reaction may produce status anginosus or precipitate congestive failure. Therefore treatment should be started gradually.

In one case untoward symptoms occurred after mercury while the patient tolerated bismuth and salvarsan, but as a rule treatments should be begun with mercury.

The author emphasizes the personal and moral element in the treatment and also the proper medical treatment of such patients as show interference with their circulation; this latter may be an important preliminary to anti-luetic treatment.

He also emphasizes that with the improved diagnostic and therapeutic technic the prognosis of aneurysm is very much improved. It is also the general impression that with systematic anti-luetic treatment the prognosis of luetic aortitis is much improved, the improvement in symptoms proceeds independently of changes in the sero-reaction.

The author has never seen improvements in the x-ray pictures after anti-luetic treatment. On physical examination there is no change.

Finally, he discusses the relative value of the various drugs and is of practically the same opinion as are the leading authorities in this country.

Hurxthal, Lewis M.: Auricular Fibrillation in Patients With Goiter. Am. J. M. Sc. 179: 507, 1930.

This report deals with 59 cases of postoperative paroxysmal auricular fibrillation and 55 cases of established auricular fibrillation treated in the Lahey Clinic. All the latter were at one time or another associated with hyperthyroidism while a few of the former followed operation for nontoxic goiters. Diagnosis was made chiefly by auscultation in the paroxysmal type while electrocardiographic tracings were used in practically all of the established group.

In most instances paroxysmal auricular fibrillation is seen following operation. It occurs frequently following removal of nontoxic goiters but more often after partial or subtotal thyroidectomy in patients with primary hyperthyroidism. It is frequently disturbing to the patient but rarely does it produce any alarming systemic

reaction. Its appearance, therefore, cannot be considered as a cardiac emergency. Treatment in most instances is indicated only for the comfort of the patient. The author believes that quinidine yields the best results in the treatment of this type of patient. It has been used only if the irregularity is distressing to the patient or if it persists after two or three days.

Approximately 10 per cent of the patients with hyperthyroidism show established auricular fibrillation. Over 90 per cent of those patients who have frank congestive heart failure associated with hyperthyroidism have this irregularity and conversely from 30 to 40 per cent of those having auricular fibrillation have a history of various degrees of this type of heart failure. Of 55 cases of this type of fibrillation, 7 stopped spontaneously and in 5 other cases quinidine was not successful. Thirty-four cases were successfully treated, 4 of which recurred. Of the 34 cases successfully treated, 30 were first given treatment after operation while 4 of these had been given quinidine successfully before thyroidectomy. Two of these recurred after the operation, and were then again successfully restored to normal rhythm. Six patients received their treatment in periods of four months to four years after operation. Iodine and thyroidectomy caused cessation in 15 per cent of all operated cases during the period of hospital observation. Iodine, thyroidectomy and quinidine resulted in a permanent return to normal rhythm in 65 per cent of all operable cases, at least for the time in which they were under observation. In hyperthyroidism uncomplicated by cardiovascular disease, return to normal rhythm may be anticipated in 100 per cent of the cases.

The selection of cases with indications and contraindications of quinidine therapy is discussed.

Weiss, Soma: The Development of the Clinical Concept of Arterial Hypertension. New Eng. J. Med. 202: 891, 1930.

This communication sketches the significant features of the evolution of the concept of hypertension and associated body changes. Emphasis is placed on the main features of this development rather than on the details of its history.

Stewart, Harold J.: The Use of Theocalcin in the Treatment of Heart Failure of the Congestive Type. J. Clin. Investigation. 8: 389, 1930.

The author has studied the effect of administration of theocalcin (theobromine-calcium salicylate) to 16 patients suffering from heart failure of the congestive type while in the hospital. The usual precautions were taken to insure standard conditions during the period of observation. In one patient nausea and vomiting seemed to indicate a toxic effect. In another case it was not possible to separate the effect of theocalcin from the simultaneous action of digitalis and urea. It was administered to one patient without signs of congestion to ascertain its effect in the absence of edema and in this patient there was no diuresis. In a second patient exhibiting edema and ascites of nephritic origin, no diuresis resulted from the administration of the drug.

Satisfactory diuresis occurred in 11 of the remaining patients. In eight, the diuresis was sufficient to free the patient of signs of heart failure and in two it was partially effective, in one it was impossible to estimate the part it played. Most of these patients suffered from arteriosclerotic form of heart disease.

While no study was undertaken to determine the action of theocalcin it is presumed that the effect is directly on the kidney. The drug can be given as long as the diuresis lasts and as long as it maintains the output of urine near the fluid intake.

The author believes that theocalcin was by far the most effective diuretic administered during this study.

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Original Communications

BUNDLE-BRANCH BLOCK WITH SHORT P-R INTERVAL IN HEALTHY YOUNG PEOPLE PRONE TO PAROXYSMAL TACHYCARDIA

Louis Wolff, M.D., Boston, Mass., John Parkinson, M.D., London, Eng., and Paul D. White, M.D., Boston, Mass.

ABERRANT ventricular complexes of the type generally recognized as indicating bundle-branch block were first produced by Eppinger and Rothberger,[3, 4] by the experimental division of the right branch of the His bundle. Eppinger and Stoerk[5] observed similar curves in five patients, and at autopsy demonstrated division of the right branch of the His bundle in two of these. The work of Cohn and Lewis,[2] and of Carter[1] indicated, however, that gross lesions of the main branches are not invariably found at autopsy in patients who during life present this type of electrocardiogram.

Following these original contributions to the subject, bundle-branch block curves have been observed as a temporary sign during infections, congestive failure, coronary thrombosis, tachycardias, and various toxic states. In most if not in all of the reported cases the abnormal curves occurred in patients with definite structural heart disease, or with extreme tachycardia. The references already cited[1, 2] indicate that the type of electrocardiogram under discussion may be obtained in the absence of gross division of a bundle branch.

Experimentally, bundle-branch block curves may be obtained in normal hearts by causing an impulse to enter one bundle branch later than the other. The same result would be produced should the impulse travel through the bundle branches at different speeds or by an aberrant course. That such a mechanism may occur in human beings with normal hearts seems likely from a study of the cases described in the present paper, the presumption being that vagal stimulation may, in certain individuals, give rise to aberrant ventricular complexes.

We have observed the occurrence of bundle-branch block curves in healthy young adults and children with apparently normal hearts. The curves may be typically those of complete right or left bundle-branch block, or of intermediate or lesser grades of aberration. Spon-

taneously, or following release of vagal tone by exercise or atropinization, there is a transition from aberrant ventricular complexes to perfectly normal ones. Coincident with the change to normal ventricular complexes, the P-R interval increases from an unusually short one (never greater than 0.1 second) to one of normal length, frequently almost doubling itself. In other words release of vagal tone is accompanied by a lengthening of the P-R interval; this paradoxical vagal effect is of considerable interest; its mechanism is obscure. Another feature observed in these patients is the occurrence of paroxysmal tachycardia, or paroxysmal fibrillation or perhaps flutter.

The phenomena just mentioned have been present more or less consistently in all of our patients. The combination constitutes a type of rhythm, or mechanism, which has not yet been described as such; it is probably not rare. Considerable importance attaches to the recognition that bundle-branch block curves do not always indicate organic heart disease. The ease with which such cases may be recognized will be apparent from the description of our cases.

CASE REPORTS

Case I. S.O.S., married, male, aged 35 years when first seen by us April 2, 1928.

Occupation. Physical director.

Chief complaint. Palpitation off and on for the past ten years.

Present history. His general health has always been excellent. Attacks of palpitation, which began ten years ago, are brought on by excitement or exertion, and once followed the drinking of one or two glasses of whiskey. During the attacks, which come on about once a week and last about half an hour, he is conscious of the heart beating rapidly and irregularly, and occasionally during these attacks he has listened to his own heart with a stethoscope, finding a grossly irregular rhythm. This has been confirmed by his physician. During the paroxysm he feels somewhat weak but continues his activity. He does wrestling, boxing, swimming and road work, running ten miles without any undue symptoms. A paroxysm of fibrillation once came on while he was swimming and ended while the swimming was continued. Less frequent attacks of a different type of palpitation occur in which the heart beats much faster and is regular except for occasional intermittence. Blood seems to rush to the head at such times. The attack is stopped by bending forward so that his head is low. Many examinations in the past fifteen years have failed to reveal any evidence of heart disease, though occasionally the heart was said to be irregular.

Active service in the army lasted from May, 1917 to August, 1919. The patient is of a "nervous," introspective type.

Past history. Negative except for Neisserian infection seventeen years ago, mild influenza in 1918, and psoriasis one year ago.

Marital history. Married five years. Wife living and well, but has never been pregnant.

Physical examination. General condition excellent. Well developed and nourished, muscular, healthy athlete in the pink of condition. The entire examination was negative except that the tonsils were large and the tip of the spleen was just palpable. *Heart.* The cardiac impulse was felt in the fifth intercostal space 7.5 cm. to the left of the midsternal line. The left border of dulness was 8 cm. and the midclavicular line was 9.5 cm. to the left of the midsternal line. The heart

rate was irregular, varying between 50 and 80 per minute, but there was a dominant rhythm. After exercise the heart accelerated moderately, but was normal in rate again in one to two minutes. The sounds were of good quality; the first apical sound was reduplicated; there were no murmurs. The pulse form and artery walls were normal. There was no arcus senilis. Blood pressure was 104 mm. mercury systolic, and 70 diastolic.

Roentgen ray report ("7 foot plate"). The heart shadow was rather round and wide acrosss the auricles, but was not "mitral shaped." The transverse diameter was within normal limits. The supracardiac shadow was small. The aorta seemed narrowed in both antero-posterior and oblique views. The measurements were as

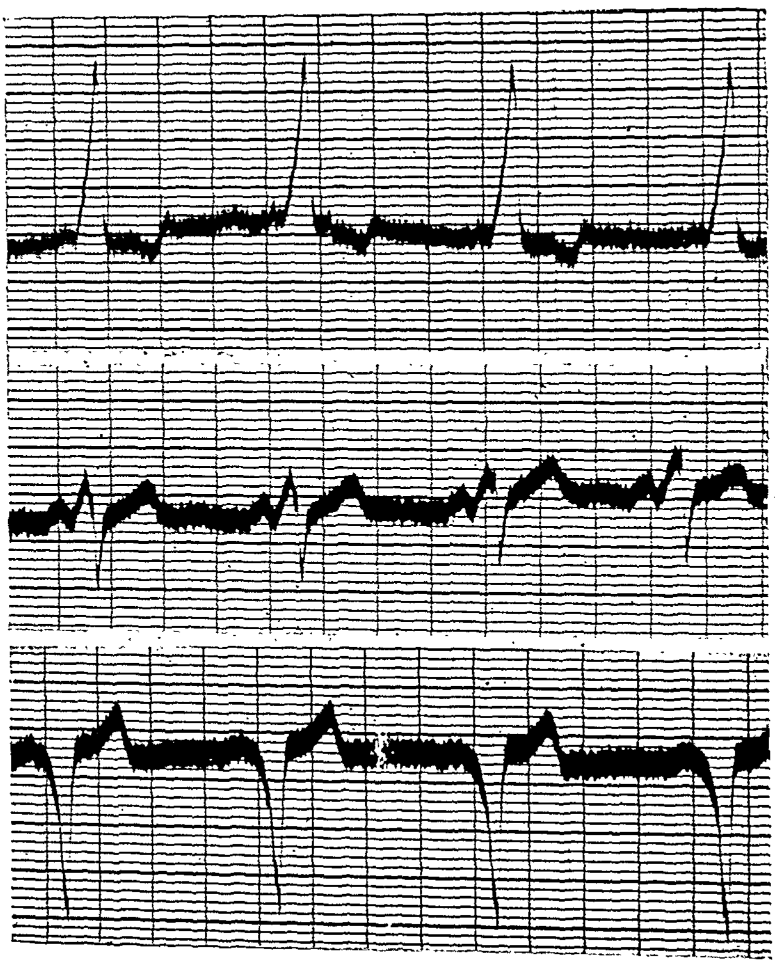


Fig. 1.—(Case I) Right bundle-branch block. The P-R interval is 0.1 second. The rate is 72. Time intervals for this and succeeding figures = 0.2 second. Horizontal lines cut off intervals of 10^{-4} volt.

follows: to the right of the midsternum 5.9 cm., to the left 8.2, total transverse diameter 14.1, length 14.5, base 13.5, width of great vessels 5.2, and internal diameter of thorax 30.5.

The blood Wassermann reaction was negative.

Later notes. (1) April 23, 1928. Is taking quinidine sulphate in daily rations of grs. ix. There have been no more paroxysms of fibrillation.

(2) June 15, 1928. In perfect health. No more paroxysms. Is not taking quinidine.

(3) August 24, 1928. Except for one or two very short paroxysms of auricular fibrillation he has been in excellent health.

(4) October 1929. He has been in excellent health, and has done strenuous athletic work. Several attacks of paroxysmal tachycardia have occurred, but none of auricular fibrillation. Physical examination negative.

Electrocardiograms. Numerous electrocardiograms were taken. When the patient was at rest the usual finding was normal rhythm at a rate of about seventy, with slight sinus arrhythmia, and intraventricular block of the "right bundle-branch type." The QRS complexes were greater than 0.1 second in duration, with the T-waves directed opposite to the chief deflection. The P-waves were poorly marked, and the P-R interval measured 0.10 second (Fig. 1). Exercise (running up and down four flights of stairs) produced a sino-auricular tachycardia rate 140-120, with

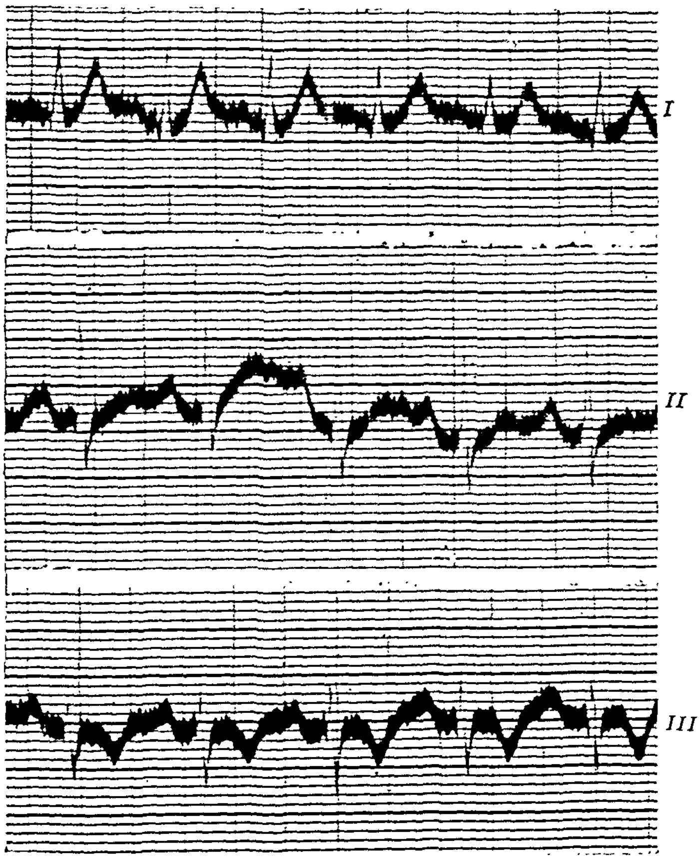


Fig. 2.—(Case I) Immediately after exercise (running up and down four flights of stairs). Sino-auricular tachycardia, rate 140 to 120. The ventricular complexes are normal, the P-waves are better marked, and the P-R interval is 0.16 second.

perfectly normal ventricular complexes throughout (Fig. 2). The P-waves were now better marked, and the P-R interval definitely longer (0.16 second). After a rest of twenty minutes the bundle-branch block complexes had returned. Following the injection of atropine sulphate (gr. 1/30 subcutaneously) the ventricular complexes again became normal, and the P-R interval measured 0.15 to 0.16 second (Fig. 3).

The last electrocardiogram, taken in October 1929, showed the normal type of complexes which changed to right bundle-branch block when pressure was exerted on the right vagus nerve.

(We are indebted to Dr. Hyman Morrison for the privilege of studying this case.)

Case II. D.C., single, male, aged 18½ years when first seen by us March 20, 1928.

Occupation. College freshman.

Present history. His general health had always been excellent. Four years ago he had his first attack of rapid vigorous heart action with sudden onset and offset, lasting fifteen minutes. The heart was regular at a rate of about 160. This had recurred from 3 to 4 times a year since, coming irregularly every few weeks to months. The attacks usually came when he was quiet, except once when he was struck in the chest in a soccer game. He lay down when an attack occurred and it quickly passed off, never lasting more than one-half hour. The last attack came three months ago while sitting at the edge of the swimming tank. A doctor who happened to be present stopped the attack by vagal pressure.

During the attacks of tachycardia there were slight dyspnea and an aching in the back of the neck. At other times there were no symptoms.

Past history and *family history* were irrelevant. He was not a blue baby.

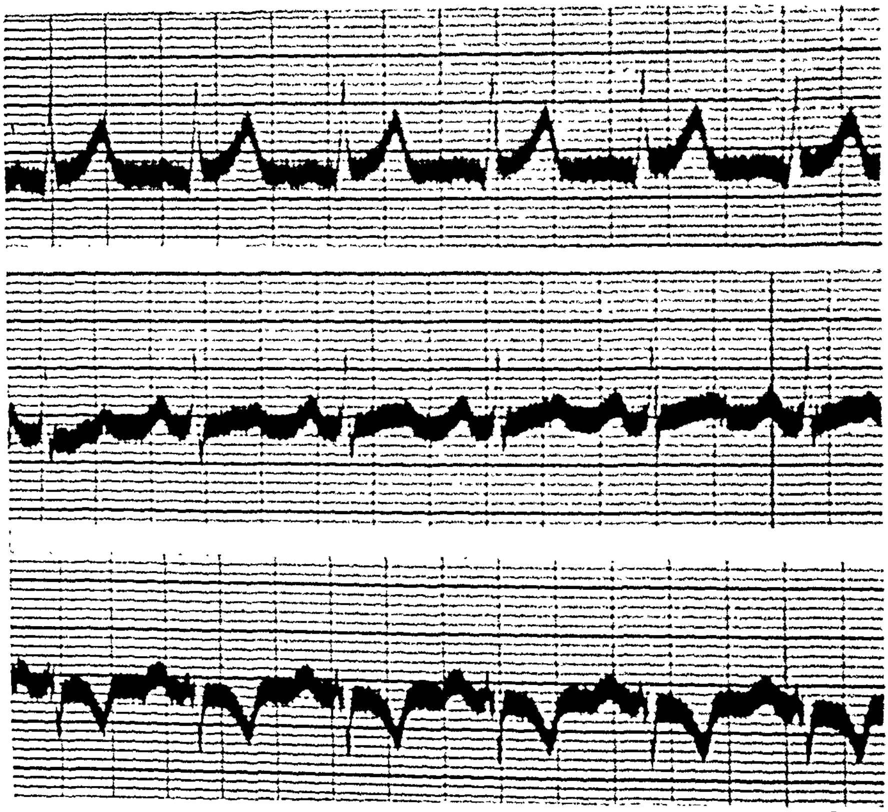


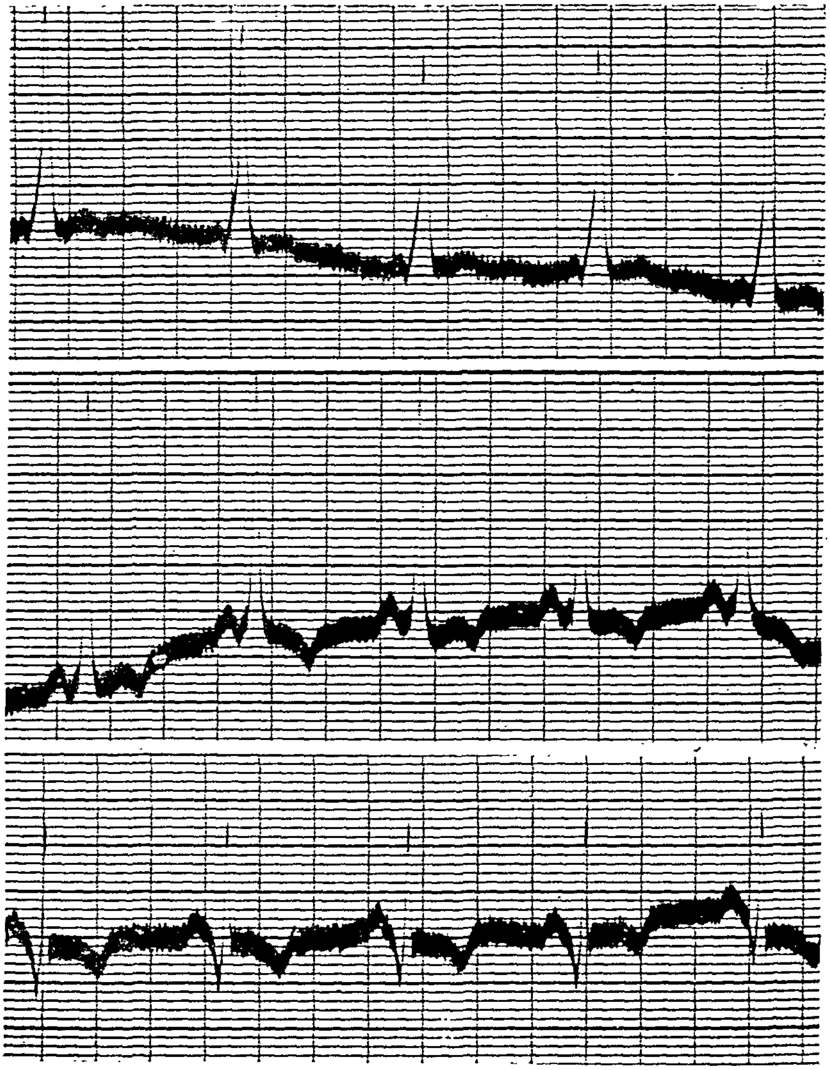
Fig. 3.—(Case I) One hour after the subcutaneous injection of 1/50 grain of atropine sulphate. The rate is 140, the ventricular complexes are normal, and the P-R interval is 0.15 to 0.16 second.

Physical Examination, which showed a large and robust athlete, apparently in excellent health, was entirely negative. The maximum apex impulse of the heart was felt behind the fifth rib, 8 cm. to the left of the midsternal line. The left border of dulness was 7.5 cm. from the midsternum and the midclavicular line was 9 cm. to the left of the midsternal line. The sounds were of good quality, the first apical sound double. At the apex a slight systolic murmur was audible when the patient was recumbent. The blood pressure was 115-120 mm. mercury systolic, and 60 diastolic. The heart rate was 68, and the response to exercise was good.

A *teleroentgenogram* ("7 foot plate") of the heart was normal.

Basal metabolism was normal.

Electrocardiograms showed aberrant ventricular complexes (intraventricular block) and an unusually short P-R interval (Fig. 4). After exercise the ventricular complexes assumed a normal physiological form and the P-R interval became distinctly longer (Fig. 5).



I

II

III

Fig. 4.—(Case II) Intraventricular block. The P-R interval is 0.1 second. Rate 96.

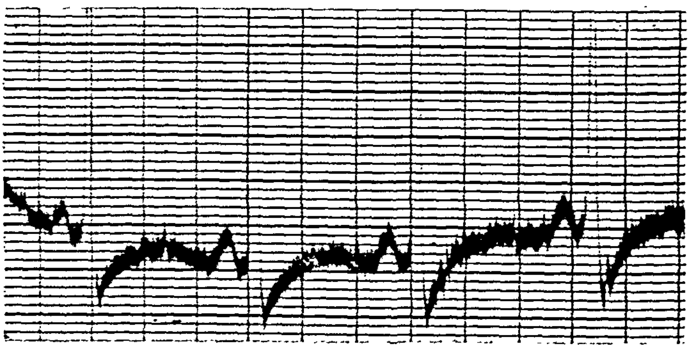


Fig. 5.—(Case II) Immediately after exercise. The ventricular complexes are normal except for deformity of the S wave and S-T interval by artefact (high resistance, resulting in over-shooting). The T-wave is upright. The P-R interval is 0.15 second Rate 96.

When last heard from in the fall of 1929 this young man was very well and active.

Case III. C.P.R., male, aged 21 years when first seen by us on June 29, 1927.

History. He complained of attacks of palpitation which had recurred ever since school days. The attacks had become more frequent so that he had one or two almost daily. They began suddenly without apparent cause, lasted from a few minutes to three hours, and stopped suddenly. Lying down or bending over usually stopped the attacks. He said that he had always been short-winded, but that he had been quite well except for the palpitation. There was no rheumatic history.

Fig. 6.—(Case III) Right bundle-branch block. The P-R interval is well under 0.1 second. The rate varies between 60 and 70.

Examination showed no abnormal signs and he looked plump and well. The blood pressure was 135 mm. mercury systolic and 80 mm. diastolic.

Radioscopy showed no enlargement.

A routine *electrocardiogram* showed right bundle-branch block, upright P-waves in all leads, and a P-R interval well under 0.1 second (Fig. 6).

On February 17, 1928 he was seen after a paroxysm of tachycardia lasting seven hours. Electrocardiograms now showed normal complexes (Fig. 7), with recurrent periods of the abnormal curve recorded in 1927. The P-waves were identical when the QRS waves were normal and when they were of the type designated as indicating bundle-branch block; the P-R interval, however, was well under 0.1 second

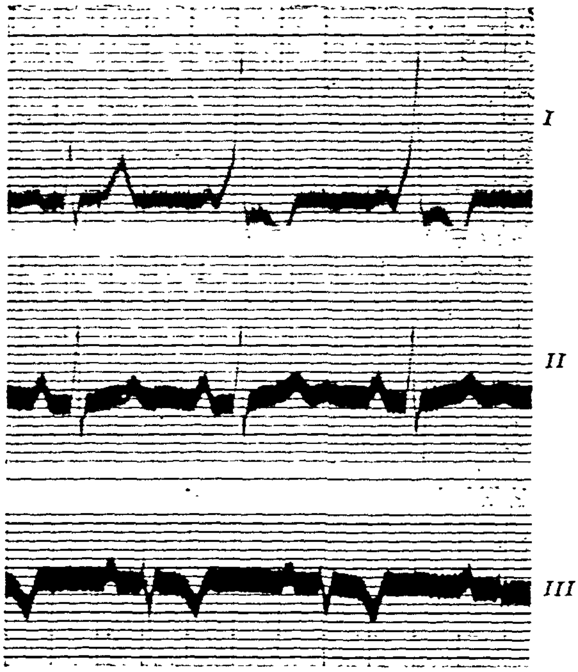


Fig. 7.—(Case III) After a paroxysm of tachycardia lasting seven hours. The ventricular complexes are normal, but occasionally there is reversion to the abnormal form. The P-R interval is almost 0.2 second. The P-waves are notched, and identical in Figs. 6 and 7.

Fig. 8.—(Case III) Two years after Fig. 6 was taken. Normal physiological curves.

when bundle-branch block curves were present, and almost 0.2 second when the QRS complexes were normal. (Fig. 7.)

On September 27, 1928, it was reported that his paroxysms were less frequent.

On the 30th of August, 1929, he was re-examined. There had been only one paroxysm of tachycardia during the previous twelve months. The electrocardiogram was now a normal physiological one (Fig. 8).

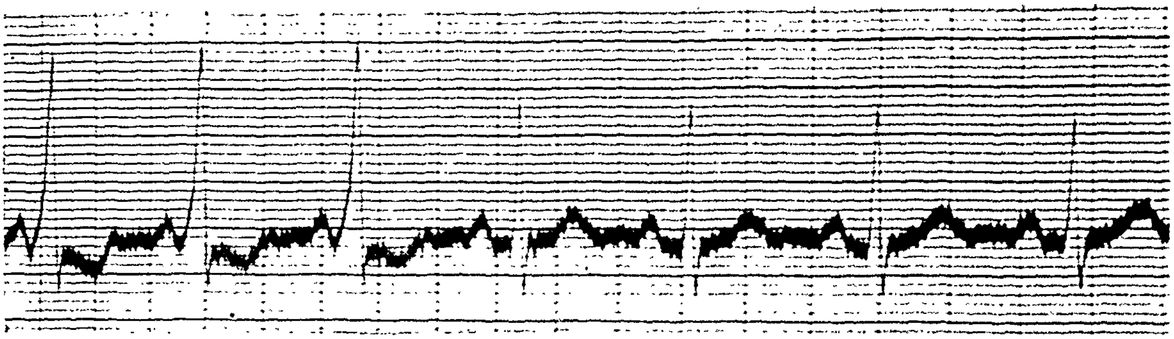


Fig. 9.—(Case IV) Spontaneous reversion from bundle-branch block curves to normal ones. The form of the P-wave remains unaltered, but the P-R interval changes from 0.09 second to 0.15 second.

Fig. 10.—(Case IV) Normal physiological complexes. P-R interval 0.15 second. In Lead II there is a transition to the abnormal form and short P-R interval.

Case IV. C.A., male, aged 16 years when first seen by us on January 7, 1926. There was a history of occasional palpitation. The heart would suddenly become rapid, generally on exertion. The last bad attack was after playing football. There were no other symptoms, and no rheumatic history.

Examination revealed no abnormal signs. The heart rate was slightly rapid, with an irregularity which at first was thought to be a sinus arrhythmia. The blood pressure was 135 mm. mercury systolic, and 75 diastolic.

Radioscopy showed no enlargement.

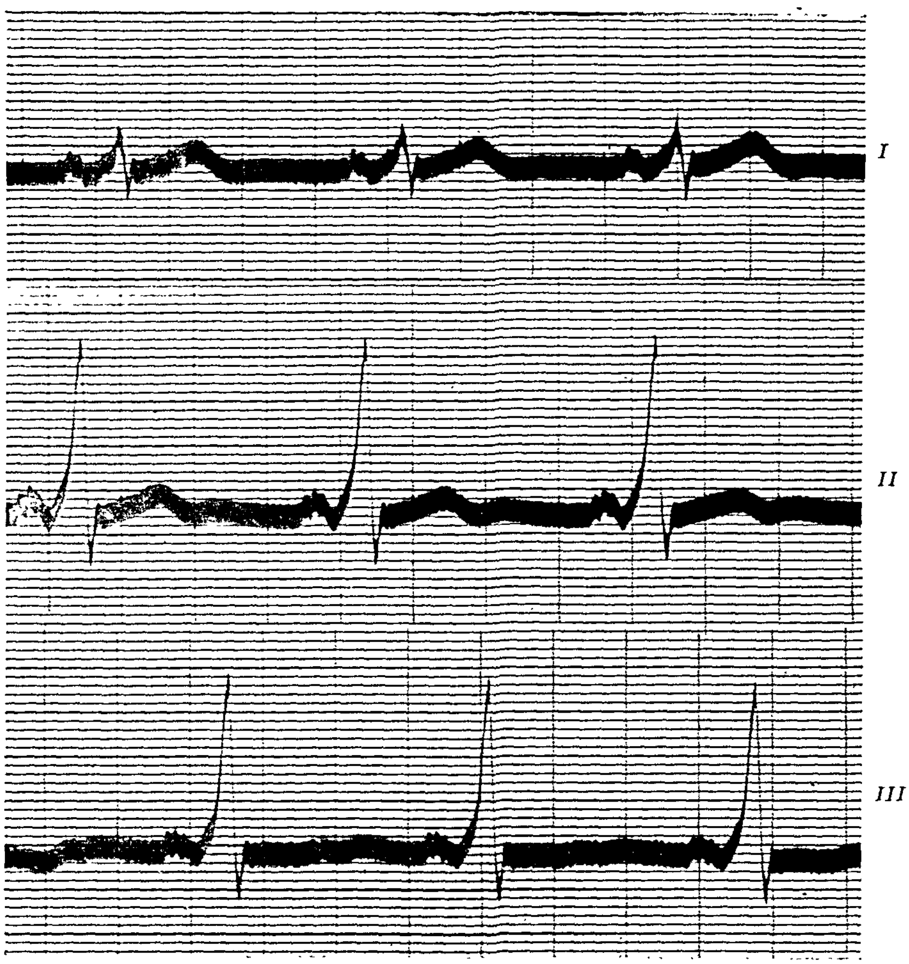


Fig. 11.—(Case IV) Bundle-branch block. The P-R interval is less than 0.1 second. The P-waves are identical in Figs. 10 and 11; note the peculiar notching of the P-waves.

Fig. 12.—(Case IV) Simultaneous electrocardiogram and jugular and radial tracings. Bundle-branch block curves are present. The a. c. v. h. sequence is normal.

Electrocardiograms. Two distinct forms of curve were obtained, one replacing the other spontaneously as shown on successive plates (Figs. 9, 10 and 11). Figure 10 shows normal physiological complexes in all leads, P-R interval 0.15 second. Figure 11 shows a special form of complex with identical normal P-waves, shortened P-R interval (less than 0.1 second), and widened QRS complexes. The respective rates are much the same, the normal about 104, the abnormal about 108 a minute.

On January 20, 1926, the abnormal type of curve was constant, and simultaneous electrocardiogram and jugular and radial tracings showed a normal a.c.v.h. sequence (Figure 12).

On February 10, 1928, the normal type of electrocardiogram was constant.

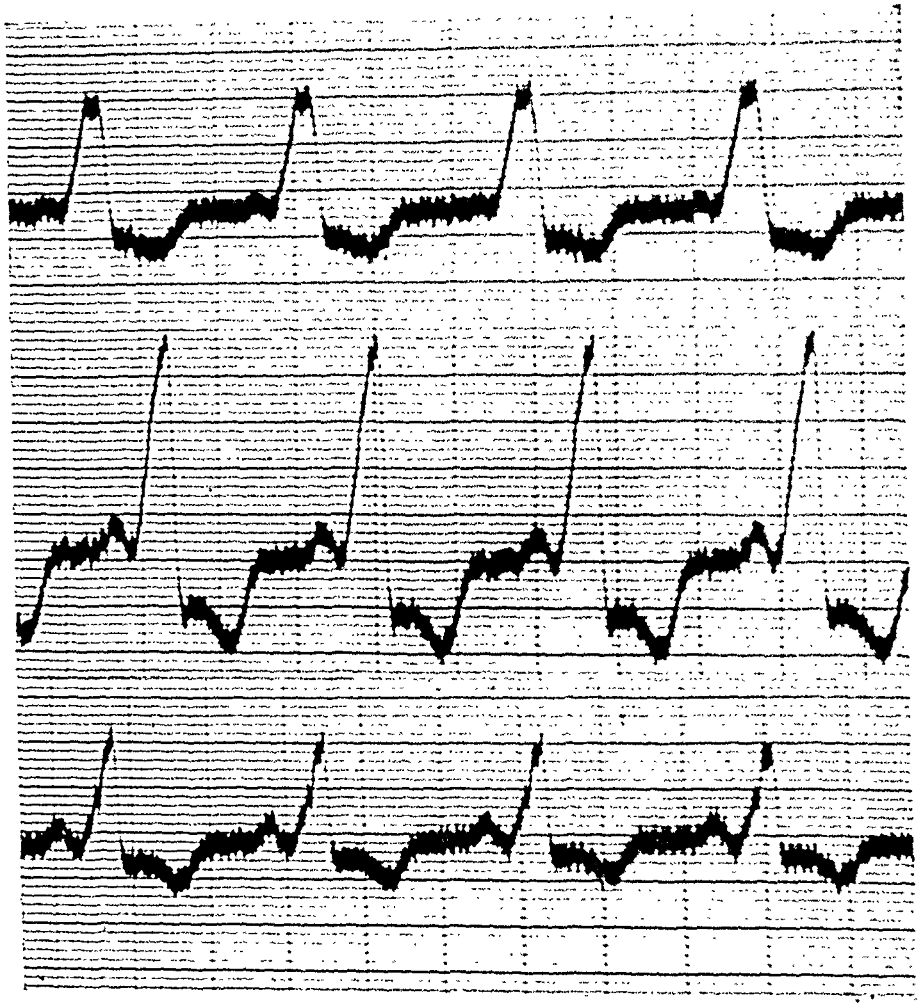


Fig. 13.—(Case V) Intraventricular block. The P-waves are normal and upright in all leads. The P-R interval is well under 0.1 second.

On October 10, 1929, the patient was examined again. He was able to play football and other games, but occasionally the heart would race at a high rate (about 200 per minute) for a few minutes. This would occur generally on exertion but once it took place in church. The electrocardiogram was now of the abnormal type.

On December 12, 1929, records showed the heart alternately in and out of the abnormal rhythm during several minutes, then the normal rhythm ruled. He was still fit and well apart from occasional attacks of palpitation.

Case V. G.H.K., male, aged 23 years when first seen by us on July 2, 1929. He complained of palpitation and slight pain in the left axilla. Once while in bed

the heart suddenly beat rapidly for a few minutes; similar attacks of palpitation occasionally occurred during the day. He played tennis and was not breathless on exertion. There was no rheumatic history.

Examination revealed no abnormal signs. The heart rate was 100 per minute. At this rate the blood pressure was 160 mm. mercury systolic, and 90 diastolic; at other times it was lower.

Radioscopy showed no cardiac enlargement.

Electrocardiograms were first taken in May, 1929, by Dr. Donald Hall of Brighton, to whom we are indebted for permission to publish the case. Our record

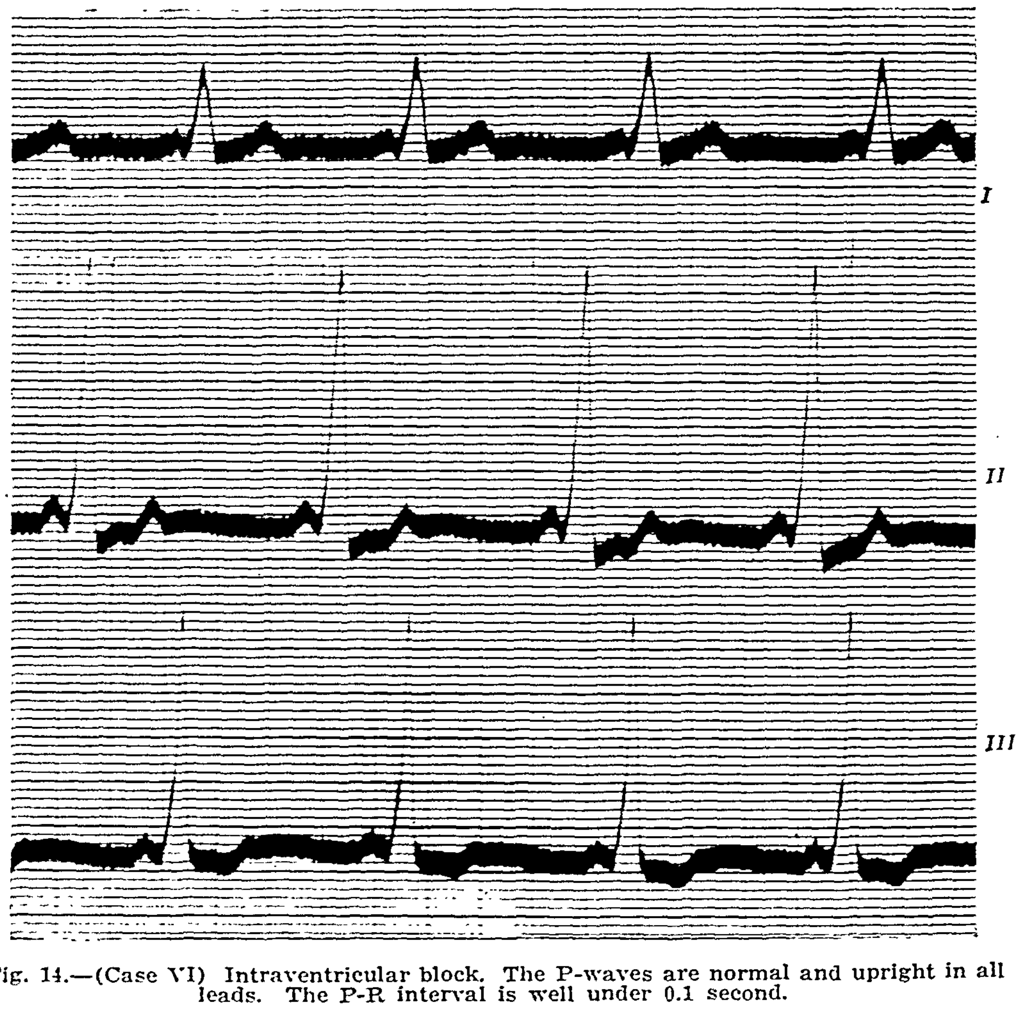


Fig. 14.—(Case VI) Intraventricular block. The P-waves are normal and upright in all leads. The P-R interval is well under 0.1 second.

of July 2, 1929, is similar (Fig. 13). The P-waves are normal and upright in all leads. The P-R interval is well under 0.1 second. The QRS complexes are wide and notched, and the T-waves are inverted in all leads.

This man was advised to continue his work as a market gardener.

Case VI. H.R.L., male, aged 23 years when first seen by us on October 8, 1928. He complained of palpitation and of slight breathlessness on exertion. At the age of 6 years he had enteric fever. There was no rheumatic history. At the age of 16 years the heart was found to be beating very rapidly and a doctor said it was enlarged. His games were restricted. Between the ages of 18 and 21 years, he was doing heavy manual work abroad without much distress. He was then rejected on medical examination, though he had only minor symptoms.

Examination revealed no abnormal signs. The heart rate was 80 a minute. The blood pressure was 130 mm. mercury systolic, and 85 diastolic.

The *orthodiagram* was normal.

Electrocardiograms showed abnormally widened ventricular complexes, regular at 60 per minute (Fig. 14). The P-waves were normal and upright in all leads. The P-R interval was just under 0.1 second. The next day, October 9, 1928, similar electrocardiograms were obtained. He was advised to disregard his occasional palpitation, but to find lighter work in view of the slight dyspnea on exertion. He proceeded abroad again.

In August, 1929, he was reported to be quite well and at work.

Case VII. B.H., male, aged 11 years when first seen by us April 13, 1929. There was a history of exhaustion, occasional pallor, and a varying pulse rate, often slow. He was always easily tired, and for a year he had had recurrent attacks in which he was pale and the pulse rate varied between 40 and 65 over a period of a few

Fig. 15.—(Case VII) Left bundle-branch block. The P-waves are normal and upright in all leads. The P-R interval is well under 0.1 second.

days. Otherwise he was fairly well and fond of games including football. Dyspnea had not been noticed. There was no rheumatic history.

Examination showed a smallish child, weighing 56 pounds; otherwise he looked well. The pulse rate was from 50 to 60 a minute and sinus arrhythmia was noted. The blood pressure was 110 mm. mercury systolic, and 75 diastolic. The heart sounds were normal and no murmurs were heard.

An *orthodiagram* showed a heart of normal size and shape.

Electrocardiograms on April 13, and again on April 16, 1929, were of the same form (Fig. 15). The P-waves were small and upright in all leads. The P-R interval was well under 0.1 second. The ventricular complexes had the form of left bundle-branch block.

Case VIII. C.B., female, aged 16 years when first seen by us on January 15, 1925. There was a history of alleged heart trouble. She had been quite well until two years before when she began to be obviously breathless at dancing and hockey. One night she felt a throbbing in her neck which kept her awake. She had im-

proved since two years ago and scarcely considered herself breathless. There was no rheumatic history.

Examination showed a girl of healthy color and appearance. There were bright red birthmarks on the left leg. There was no clubbing of the fingers. The heart sounds were normal. The blood pressure was 110 mm. mercury systolic, and 75 mm. diastolic.

Radioscopy showed slight to moderate enlargement of the heart to the right, with active systolic pulsation of the right and left borders; the diaphragm moved well.

A brisk walk with the patient showed that she was more breathless than a healthy observer.

Electrocardiograms showed a regular rhythm at a rate of from 60 to 70 a minute (Fig. 16). The P-waves were normal and upright in all leads. The P-R interval

Fig. 16.—(Case VIII) Right bundle-branch block. The P-R interval is well under 0.1 second.

was well under 0.1 second. The ventricular complexes had the complete characteristics of right bundle-branch block. On January 16, 1925, the following day, exactly similar records were obtained.

Three years later, at the age of 19, she was reported to be in good health and hard at work as a student.

Recently (October 11, 1929) she has been seen again, at the age of 21 years. She is a university student, and is active and well. Her only complaint is that she is easily tired. Physical examination and radioscopy show no abnormalities. The electrocardiogram is now normal (Fig. 17) in contrast with that taken in 1925 (Fig. 16).

Case IX. H. H., male, a musician, aged 42 years when first seen at the London Hospital on the 28th of May, 1914. He complained then of attacks of palpitation, which began at the age of nine years. They were sudden in onset and offset, and

their duration varied from a few minutes to two weeks. Frequently the attacks could be stopped if the patient held his breath or put his head between his knees. Otherwise he was well.

There was no rheumatic history. He had diphtheria and scarlet fever some years after the onset of the attacks of paroxysmal tachycardia.

Examination when first seen, which was on the tenth day of an attack of

Fig. 17.—(Case VIII) Three years later. Normal physical curves. The P-R interval is 0.16 second. The P-waves are identical in Figs. 16 and 17.

Fig. 18.—(Case IX) Intraventricular block. The P-R interval is 0.1 second. Time intervals = 0.2 and 0.04 seconds.

paroxysmal tachycardia showed dyspnea, a large heart, dulness and crepitations at the lung bases, and a large pulsating liver. The blood Wassermann reaction was negative.

Electrocardiograms taken after the paroxysm ended showed a regular rhythm with upright P-waves in all leads, a short P-R interval, abnormally widened QRS complexes and inverted T-waves in all leads (Fig. 18). An electrocardiogram was

obtained during a paroxysm of tachycardia at a rate of 150, the form of the curve being unlike that between attacks.

He was examined again on the 15th of September, 1914. The last paroxysm had occurred six weeks before and lasted three weeks. There was cardiac enlargement both on physical examination and by radioscopy. There were no murmurs. The lungs were normal.

Between the ages of 47 and 57 years he had no attacks. In 1928 the paroxysms returned. The heart was enlarged (radioscopy). An electrocardiogram between attacks was in general like that taken in 1914, as was another obtained during a paroxysm.*

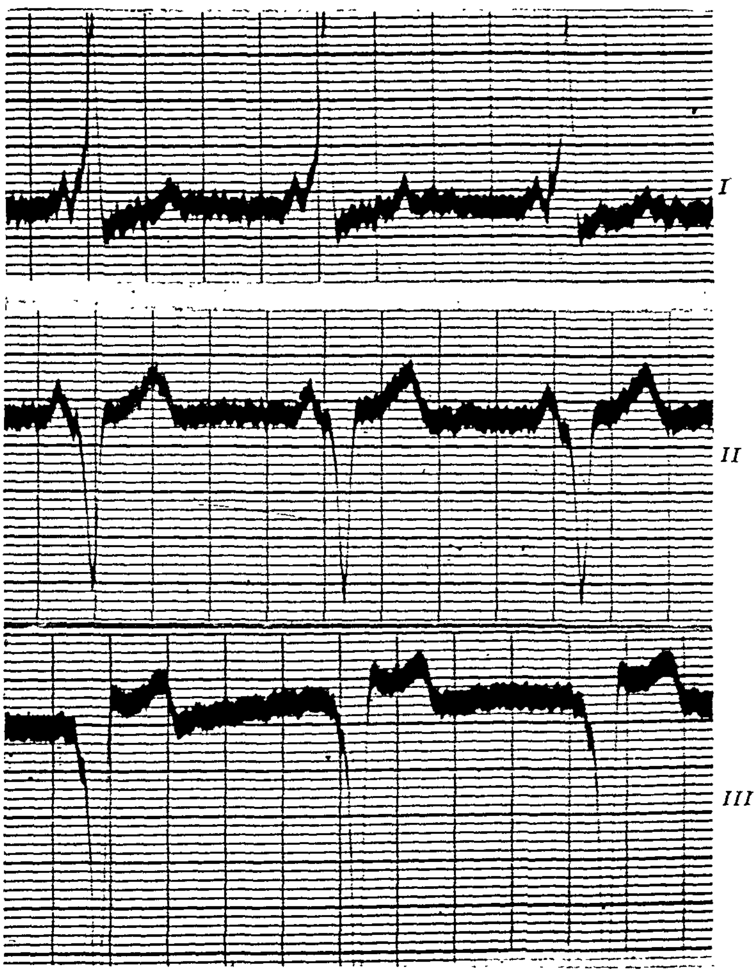


Fig. 19.—(Case X) Intraventricular block. The P-R interval is 0.1 second.

Case X. Mrs. A. C. M., a widow, aged 44 years when first seen in the Out-Patient Department of the Massachusetts General Hospital on November 26, 1927. She complained of attacks of palpitation. The attacks, which began at the age of 7, were always sudden in onset and offset. For the three years from 1924 to 1927 they had occurred more frequently, often daily. They lasted from a few minutes to several hours (intermittently) and were easily terminated by taking a deep breath and holding it, or by lying down.

*The patient's present condition has been described recently in a paper by Dr. Francis Bach entitled, "Paroxysmal Tachycardia of 48 Years' Duration, and Right Bundle-Branch Block." Proc. Roy. Soc. Med. London, 22: 412, 1929.

She had measles and diphtheria at the age of 5 years. In 1923 she had had her tonsils removed because of recurring tonsillitis and peritonsillar abscess. There was no rheumatic history.

Physical examination was entirely negative. The blood pressure was 140 mm. mercury systolic, and 85 diastolic.

Electrocardiograms showed a regular rhythm at the rate of 65 a minute (Fig. 19). The P-waves were normal and upright, and the P-R interval was 0.1 second. The ventricular complexes were of the type designated as indicating right bundle-branch block.

She was again seen on December 29, 1927, in an attack of paroxysmal tachycardia. The heart rate was over 200 and regular. An electrocardiogram was taken which showed auricular paroxysmal tachycardia at a rate of 230, without A-V block.

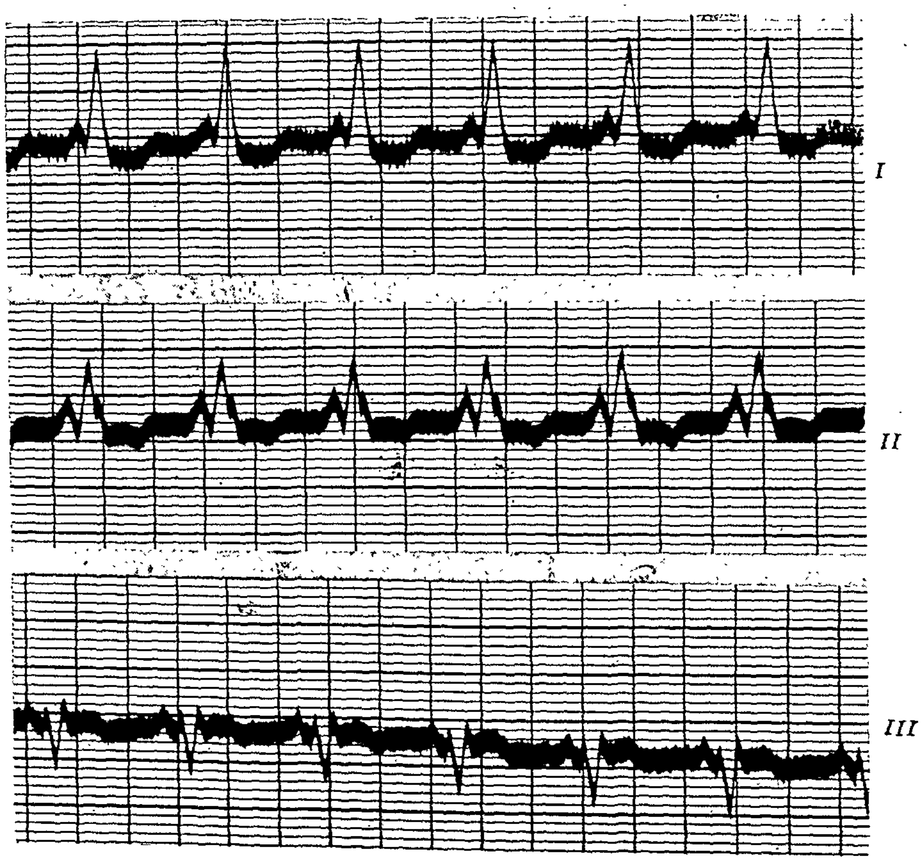


Fig. 20.—(Case XI) Intraventricular block. The P-R interval is less than 0.1 second.

The ventricular complexes were normal in form. After the electrocardiogram was taken she ended the attack by a forced inspiration. She then had frequent premature beats. She stated that since taking quinidine the attacks had become less frequent.

Case XI. Mrs. R. E., aged 55 years, entered the West Medical Service of the Massachusetts General Hospital on February 26, 1918, complaining of palpitation. The attacks of palpitation had begun ten years previously, but for the past four years the attacks had been somewhat more severe, occurring with change of weather to wet and cold, as well as after any indiscretion in diet. For two months prior to entrance into the hospital attacks of palpitation had been occurring at night, waking her out of sleep. As a rule the attacks lasted ten minutes.

There was no rheumatic history. She had had tonsillitis every year during youth. For a year there had been slight localized edema of the legs. She considered herself nervous.

Physical examination showed a poorly nourished, cyanotic, uncomfortable woman. The heart was moderately enlarged, the systolic blood pressure varied between 175 and 205 mm. mercury, the diastolic between 95 and 105. There was a loud apical systolic murmur transmitted to the axilla. There were signs of pulmonary tuberculosis.

The blood Wassermann reaction was negative.

Roentgen ray examination showed cardiac enlargement and pulmonary tuberculosis.

The *electrocardiogram* revealed normal P-waves which were upright in all leads. The P-R interval was less than 0.1 second. The ventricular complexes were of the type designated as indicating bundle-branch block (Fig. 20). The rhythm was regular and the rate 114.

DISCUSSION

The combination of bundle-branch block, abnormally short P-R interval, and paroxysms of tachycardia (also paroxysmal auricular fibrillation and perhaps flutter) in young, healthy patients with normal hearts is distinctive, and worthy of recognition as a mechanism heretofore undescribed as such. The reversion to normal ventricular complexes and longer (normal) P-R interval, spontaneously or by vagal release following exercise or atropinization is characteristic. The paradoxical effect of vagal stimulation on the P-R interval is noteworthy.

We have been unable to demonstrate structural heart disease in our patients, except in the two oldest ones. One of these (Case IX) was first seen at the age of 42 years; he then had had paroxysms of tachycardia for 33 years. An electrocardiogram showed bundle-branch block with abnormally short P-R interval. Fourteen years later his electrocardiogram was essentially unaltered. The abnormal cardiovascular signs on physical examination in this patient may have been the result of coincidental development of organic heart disease. The other patient (Case XI) was 55 years old when first seen, and on account of her age and the presence of hypertension, we believe that the abnormal cardiovascular signs were probably coincidental and not associated with the peculiar mechanism, already described, present in this case.

None of our patients presented evidence or gave a history of rheumatic infections. Other infections, toxic states, and rapid heart rates were not responsible for the abnormal electrocardiograms. The subjects were in good health, and as a rule the only complaint was palpitation. The age of our patients suggests that a congenital anomaly may be responsible for the phenomena observed in this group. We have no proof for or against this suggestion. All the available evidence points to vagal influence as the controlling factor in this mechanism. Incidentally, it may be pointed out that here is a group of patients in whom paroxysmal tachycardia and auricular fibrillation (and perhaps flutter) is obviously associated with this unusual mechanism, quite possibly of vagal origin.

A case undoubtedly exhibiting the same mechanism was described in 1921 by A. M. Wedd.[6] A student, 19 years old, had had paroxysms of

tachycardia since the age of 5 years. He was well otherwise and the heart and blood pressure were normal. Electrocardiograms showed intraventricular block and a P-R interval of 0.08 second. The P-waves were upright in all leads. At other times the ventricular complexes were normal, and the P-R interval doubled. The author assumes the presence of A-V nodal rhythm.

A somewhat similar case was reported by F. N. Wilson in 1915.[7] This patient had mitral stenosis, and the author suggests that it is "improbable that the bundle-branch block was due to vagus influence alone," but that "conduction through the right branch of the A-V bundle was already impaired and that this rendered it especially susceptible to vagus influence." The short P-R interval was explained by assuming that A-V nodal rhythm was present; the P-wave was inverted in Leads II and III.*

A study of the electrocardiograms of our patients has enabled us to exclude the presence of A-V nodal rhythm because frequent ventricular premature beats were followed consistently by compensatory pauses, and the form of the P-waves occurring with both long and short P-R intervals was identical. In several patients the P-waves were distinctly notched, making identification easy and certain. Finally, the P-waves were always upright in all three leads.

The group includes eight males and three females. The youngest patient was eleven years old when first seen. Two patients were 16, one 18, one 21, two 23, one 35, and the three oldest patients were 43, 44 and 55 years respectively. One patient had attacks of paroxysmal tachycardia for 48 years, another for 37 years, one for 14 years, and two patients for 10 years respectively.

SUMMARY AND CONCLUSIONS

1. Eleven cases are here reported of an unusual cardiac mechanism, heretofore undescribed as such, consisting of functional bundle-branch block and abnormally short P-R interval, occurring mostly in otherwise healthy young people with paroxysms of tachycardia or of auricular fibrillation.

2. Spontaneously, or following release of vagal tone by exercise or atropinization, the ventricular complexes revert to the normal physiological form, and the P-R interval lengthens to become normal.

3. Vagal influences seem to be largely responsible for the mechanism described. A paradoxical effect of vagal stimulation on the P-R interval has been observed.

4. Infection, rheumatic and otherwise, toxic states, and rapid heart rates are not responsible for the abnormal electrocardiogram. Auriculo-

*Recently W. W. Hamburger in the Medical Clinics of North America (13: 343, 1929) reported the occurrence of bundle-branch block with a short P-R interval in a child aged four and one-half years, who had had paroxysmal tachycardia for one year. The author assumed that acute severe right bundle-branch block occurred as the result of an acute respiratory infection.

ventricular nodal rhythm is apparently not responsible for the short P-R interval.

5. From a study of the cases here presented we conclude that:

a) Aberrant ventricular complexes of the type generally recognized as indicating bundle-branch block may occur in healthy people with normal hearts.

b) Vagal stimulation is capable of altering markedly the form of the ventricular complex, and may be responsible for the occurrence of complete bundle-branch block curves in apparently normal hearts at normal rates of beating.

c) Vagal stimulation may shorten markedly the P-R interval without the production of A-V nodal rhythm, and without dislocating the auricular pacemaker.

d) In the group of cases reported paroxysmal tachycardia and auricular fibrillation are associated with the nervous control of the heart.

e) The recognition of functional bundle-branch block is of considerable practical importance. The combination of intraventricular block with abnormally short P-R interval, interchangeable with normal ventricular complexes with longer P-R interval (reversion spontaneous or following exercise or atropinization) in healthy young people with paroxysmal tachycardia (or auricular fibrillation) is distinctive.

f) This mechanism is apparently not indicative of disease of the heart.

NOTE: In this paper bundle-branch block when mentioned is referred to according to the old nomenclature of right bundle-branch block for upright widened Q-R-S waves in Lead I and inverted widened Q-R-S waves in Lead III, and left bundle-branch block for inverted widened Q-R-S waves in Lead I, and upright widened Q-R-S waves in Lead III according to the newly revised nomenclature, which is probably correct, these designations would be changed, so that one should read ''left bundle-branch block'' for ''right'' and ''right bundle-branch block'' for ''left'' in this paper.

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THE SUBSEQUENT COURSE AND PROGNOSIS IN CORONARY THROMBOSIS

An Analysis of 287 Cases*

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With a growing understanding of the clinical picture of acute coronary closure it has become increasingly evident that a considerable proportion of such patients survive their first attack and that some of these thereafter enjoy reasonably good health for a good many years. It was in the hope of throwing some further light upon the fate of such patients as have lived through one attack that this study of a large number of cases of coronary thrombosis was undertaken.

The material for this study has been assembled from three different sources: the private records of one of the writers (117 cases); the two medical services of the New York Hospital† (119 cases); and the medical department of the Out-Patient Clinic of the Cornell Medical College (51 cases). It has seemed probable that material gathered from these three sources would present a fairly accurate picture of the disease as it is seen in the different social and economic strata of the community.

Although the diagnosis in most of the cases was not confirmed by autopsy (there were 31 autopsies among the 48 patients dying in the hospital), we feel quite certain that only cases with acute coronary closure and cardiac infarction have been included in this study. Cases in which there seemed the slightest doubt as to the accuracy of the diagnosis have been excluded. This statement applies especially to the so-called atypical clinical types in which pain is usually an inconspicuous feature. Only one case presenting the picture of acute pulmonary edema has been included, and in that instance the diagnosis was confirmed by necropsy. On the other hand it seems reasonably certain that by following this rule strictly a considerable number of genuine instances of thrombosis have been rejected. After all there are few diseases which offer more opportunities for the ultimate confirmation of the clinical diagnosis, even without autopsy, than does the one under consideration.

SEX

Among the 287 cases analyzed 243, or 84.7 per cent occurred in men and 44, or 15.3 per cent, in women. This ratio corresponds fairly well

*Read at the meeting of the Association of American Physicians at Atlantic City, May, 1930.

†The authors are greatly indebted to Dr. W. R. Williams for permission to include in this study, cases from the Second Medical Division of the New York Hospital.

with that of other statistics and with the generally accepted view that the disease is many times more frequent in men than in women.

AGE AT FIRST ATTACK

An analysis of the age incidence at the time of the first attack was begun rather as a perfunctory duty and without any expectation that the figures would disclose anything of special interest, but it soon became apparent that the tabulation revealed facts which were both surprising and suggestive. It should be emphasized that the figures given represent the age at the time of the first attack and not necessarily that at the time of the attack in which the patient was seen. Such statistics we believe have hitherto never been presented.

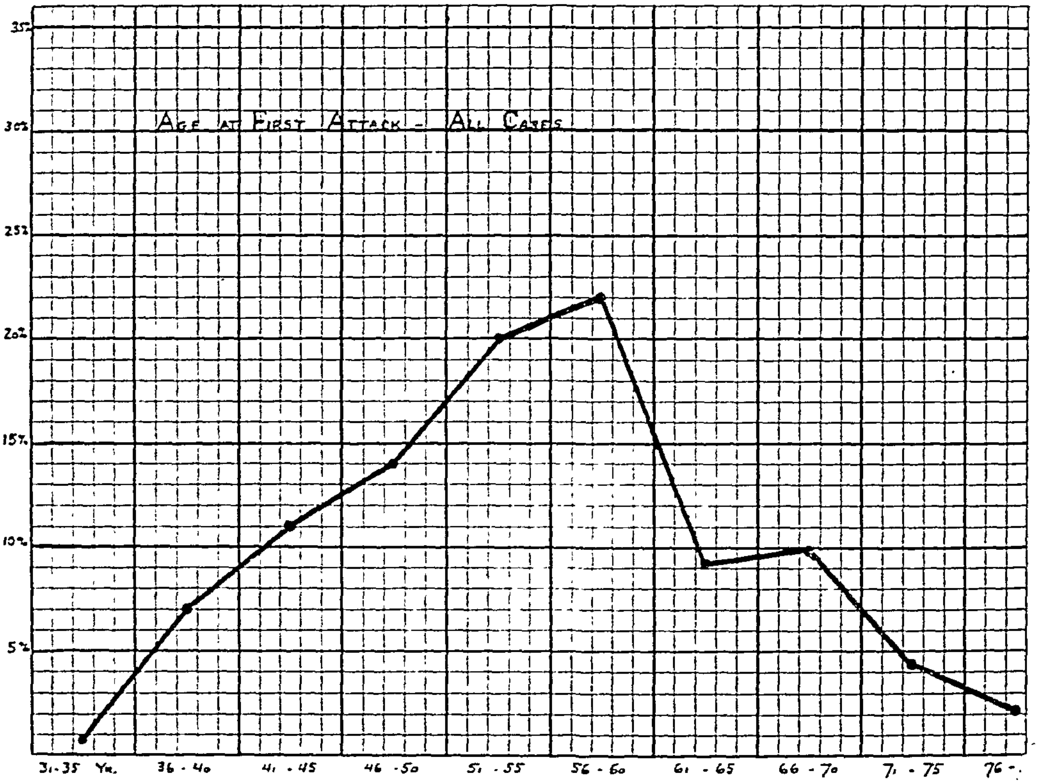

Fig. 1.

In Fig. 1 are plotted, in percentages of the total number, the ages of all the patients arranged in five-year periods. It will be seen that the curve of incidence rises steadily and almost uniformly from the 31-35 year period to reach its maximum height in the 56-60 year period, after which it falls very abruptly. Furthermore it will be seen that 75 per cent of the patients have had their first attack before the sixty-first year and only 25 per cent after that time; that the incidence is distinctly greater in the 41-45 year period than in either of the five-year periods in the decade between 60 and 70, and that the percentage of cases having their onset in the 36-40 year period is considerably greater than that having their onset in the years between 71 and 75. These figures seem

to point conclusively to the fact that coronary thrombosis is a disease which usually has its onset, not in the later years of life, but rather in the years between 40 and 60. In encountering instances of undoubted coronary thrombosis in the decade between 40 and 50 it has been customary to look upon them as distinct exceptions to the general rule. In the present series, however, no less than one-third of all the patients had their first attack before the fifty-first year; and one is forced to conclude, if this series can be accepted as representative, that such precocious cases constitute an important fraction of the whole number and cannot be regarded as in any way exceptional.

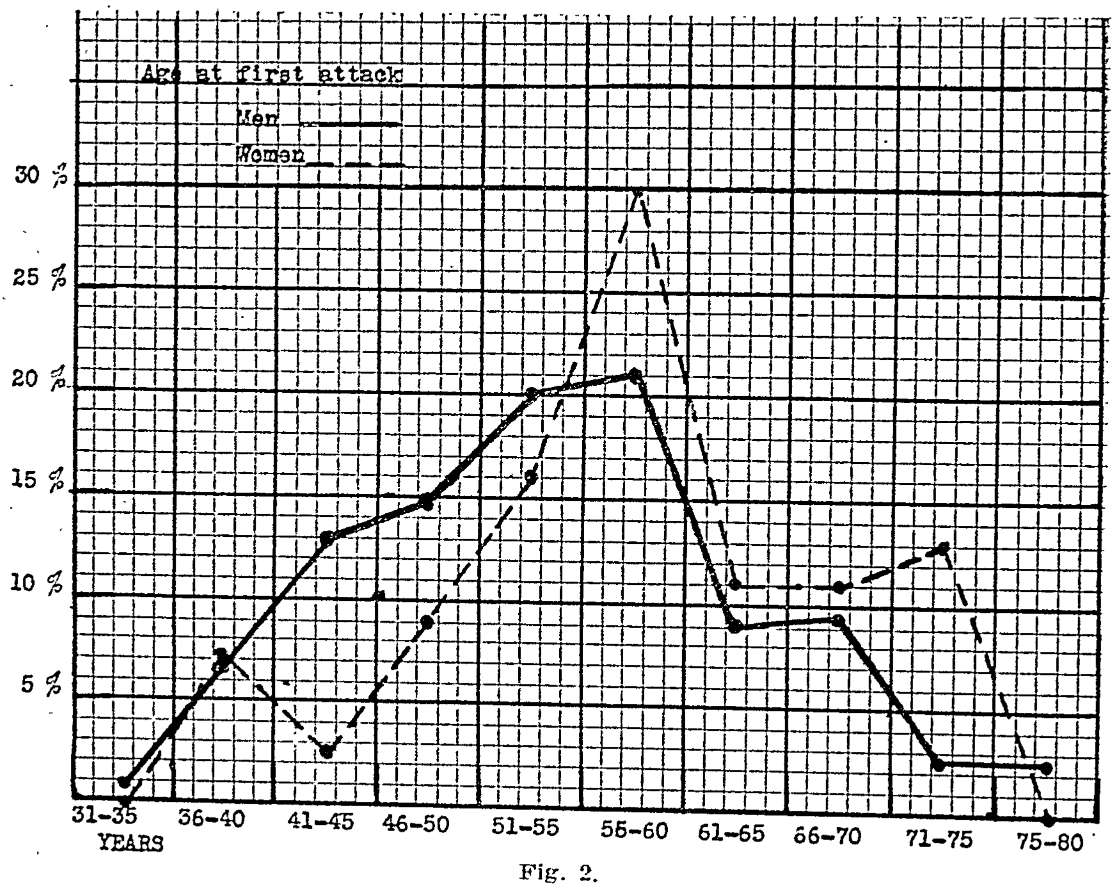

Fig. 2.

If then one assumes that local arteriosclerotic changes in the coronary arteries or their branches represent an essential factor in the production of thrombosis, the conclusion seems unescapable that, often at least, visceral arteriosclerosis must begin at a much earlier age than we have been accustomed to believe. Although not directly pertinent to the subject of the paper, this evidence pointing to the frequency of sclerotic changes in the coronary branches in early middle life seems to the writers one of the most important and most suggestive facts that this analysis has brought to light.

COMPARISON OF AGES AT FIRST ATTACK OF MEN AND OF WOMEN

In Fig. 2 are plotted separately the age incidences in five-year periods of the first attack in men and in women. It will be seen that

whereas the curve for men, as was to be expected, corresponds very closely with that for all the cases (Fig. 1), the curve for women shows distinct differences. There is a noticeable lag in the curve during the earlier five-year periods, a sudden sharp peak (30 per cent) in the 56-60 year period and a distinctly greater proportion of cases in the later years of life.

ASSOCIATION OF CORONARY THROMBOSIS WITH ARTERIAL HYPERTENSION, SYPHILIS AND DIABETES

Among the 274 patients in whom the information was available, preexisting disease, in the form of arterial hypertension, syphilis or diabetes, was recorded as follows:

Arterial hypertension in 93 cases, or 33.9 per cent.
Syphilis (proved or probable) in 39 cases, or 14.2 per cent.
Diabetes in 28 cases, or 10.2 per cent.

In view of the widespread belief that persistent high blood pressure is much the most important predisposing factor to coronary disease, the low figure given above for hypertension (34 per cent) will come as a surprise to many. Without insisting upon the accuracy of these figures (since they represent only those patients *known* to have had preexisting hypertension) it nevertheless seems reasonably certain that such hypertension cases made up, at the most, not more than half of the total number. In the series of 100 cases reported by Parkinson and Bedford[1] there were 15 patients with an antecedent systolic blood pressure of 200 mm. or over and 34 patients with systolic pressures ranging between 150 and 200 mm.—a total of 49 per cent. Among the 145 patients studied by Levine,[2] 58 (or 40 per cent) were known to have had an antecedent hypertension. Nevertheless Levine concludes "that a distinct hypertension existed as a forerunner of coronary thrombosis in the majority of cases"; basing this conclusion upon the fact that "many patients with normal blood pressures showed retinal changes of a sufficiently well marked degree to indicate that a previous hypertension had existed."

We, ourselves, have for a long time been much impressed by the frequency with which coronary thrombosis appears in individuals whose blood pressures have remained *low* and have failed to show the usual tendency toward gradual increase with increasing years, and we have formed the impression that the disease is to be found among such persons almost as frequently as among those with hypertension. In the present series the records available are not sufficiently full either to confirm or to disprove that impression.

COMPARISON OF AGES AT FIRST ATTACK OF HYPERTENSION CASES WITH THOSE FOR ALL CASES

In Fig. 3 are plotted separately the percentages of age incidence, in five-year periods, of cases of pre-existing hypertension and of all cases. The curve for the hypertension cases, as compared with that for all cases, shows a distinctly smaller incidence in the five-year periods up to and including the 51-55 year period, and a somewhat increased incidence in the 66-70 year period.

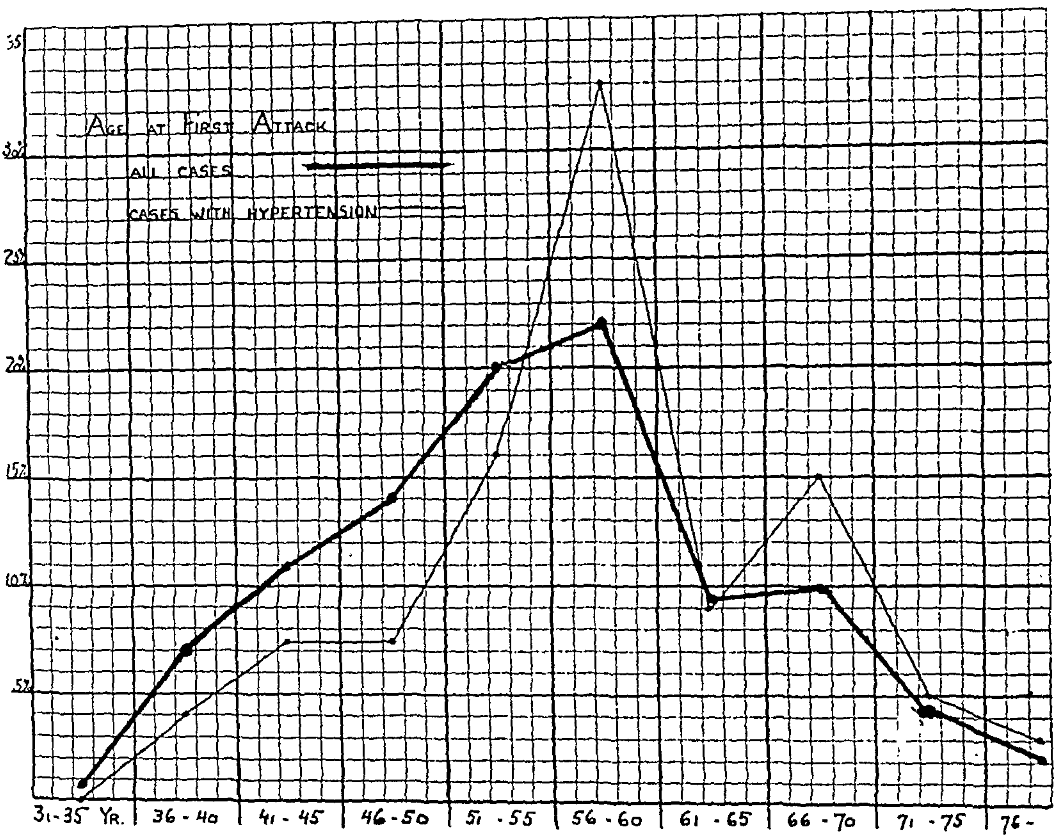

Fig. 3.

COMPARISON OF AGES AT FIRST ATTACK OF CASES WITH SYPHILIS WITH THOSE FOR ALL CASES

Syphilis, either proved or probable, was found in 39 patients, or 14.2 per cent of 274 patients. The "proved" cases included those with either definite physical signs of syphilis or with a clear history of that disease. Patients in whom there was only a positive Wassermann reaction were classed as "probable." Fig. 4 shows the graph of the age incidences of the first attack in cases with syphilis in comparison with that for all cases. Although the differences between the two are not great, there is among the syphilitic cases an appreciable shift of the curve toward the earlier age groups. How significant this shift may be is questionable in view of the fact that in most instances, even among the cases with syphilis, we have no proof that the lesions in the coronary vessels were actually of a luetic nature. Certainly the earlier belief that

the precocious cases of coronary thrombosis usually have a syphilitic basis is no longer tenable, for in most of the early cases in this series there was no evidence whatever of an antecedent luetic infection.

COMPARISON OF AGES AT FIRST ATTACK OF CASES WITH DIABETES WITH THOSE FOR ALL CASES

Trustworthy evidence of a pre-existing diabetes at the time of the first attack of coronary thrombosis was obtained in only 28 patients, or 10.2 per cent of 274 cases. This figure was unexpectedly low, and it seems probable that it is below the true incidence of that disease as it

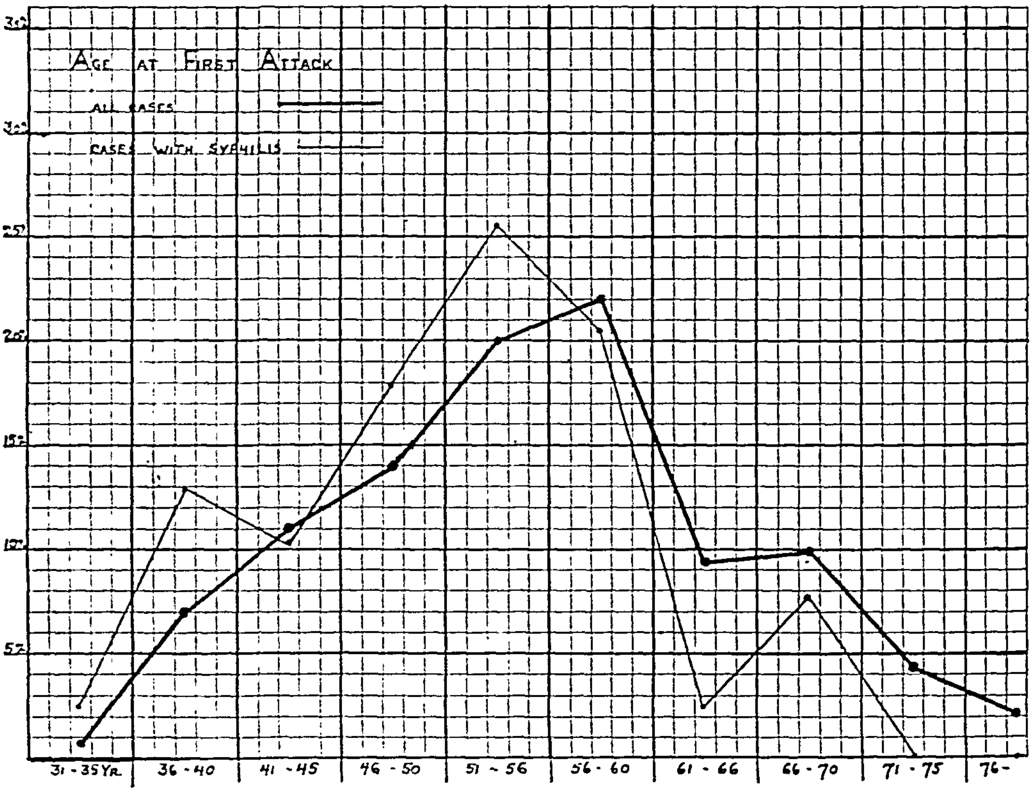

Fig. 4.

is found associated with coronary thrombosis. It is quite probable that in some instances a more thorough investigation might have revealed a latent diabetes. Levine, in his series of 145 cases of coronary thrombosis, found evidence of diabetes in 34 cases, or 23.7 per cent.

In Fig. 5 is plotted, by five-year groups, the age incidence at the time of the first attack, of the cases complicated by diabetes in comparison with that for all cases. The small number of cases with diabetes renders such a comparison of doubtful value, but the chart shows an interesting concentration of the diabetic cases in the age groups between 50 and 60 years, and a correspondingly smaller percentage of cases in the earlier and later age groups. Just what the significance is of this association of diabetes with coronary disease is still uncertain. It

seems probable, however, that diabetes is not, in itself, a predisposing cause of coronary thrombosis but that both of these conditions are the separate expressions of a single underlying cause—visceral arteriosclerosis.

GENERAL STATISTICS

Before taking up a detailed analysis of the fate of the patients included in this study, it is desirable to present a few general statistical figures. Of the 287 patients whose records were reviewed, 117 are known to be living at the present time and 142 are known to have died. In the case of the remaining 28 patients, it has been impossible to trace

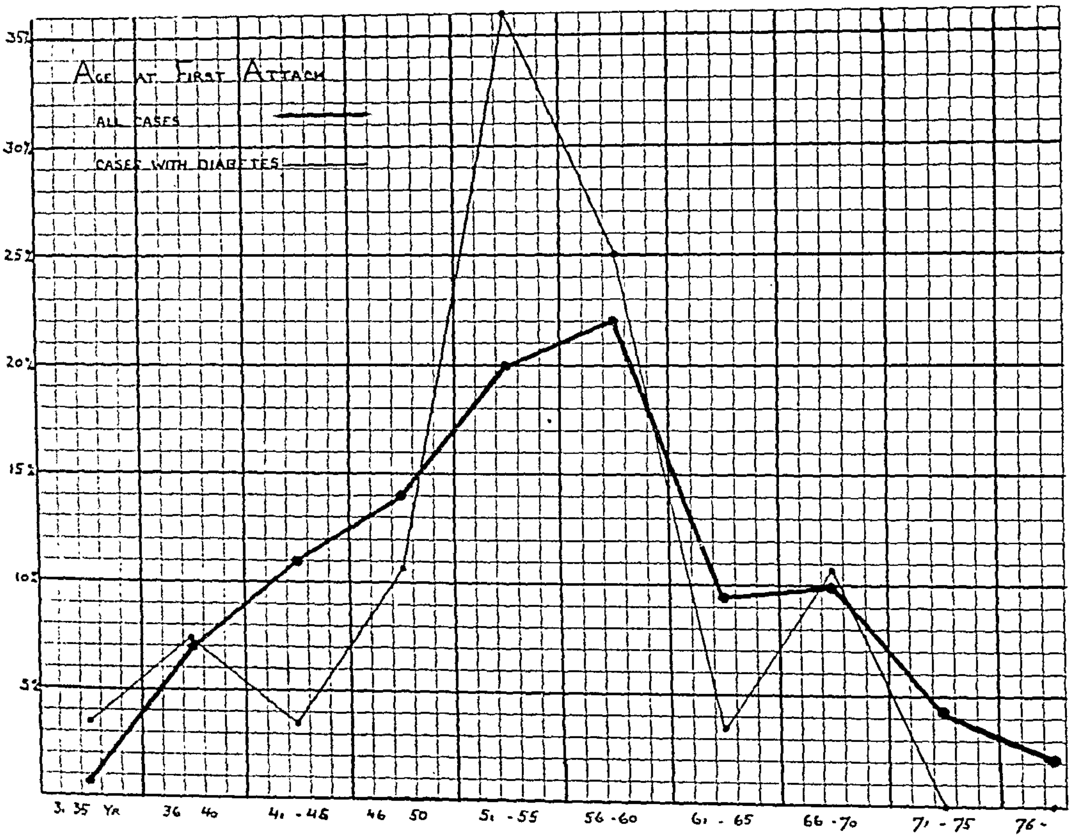

Fig. 5.

them, and their fate is unknown. That is to say, of the 259 patients concerning whom there is definite information, 45 per cent are living and 55 per cent have died. Three patients in their first attack left the hospital as soon as the severe pain had subsided and have been lost, so that it is not known whether they survived even their initial attack. Of the 142 patients who have died, 46 succumbed during their first attack. This gives an immediate mortality in the initial attack of 16.2 per cent* (of 284 cases). This percentage of deaths in the first attack is surprisingly low—much lower than is usually represented. Among

*In estimating the immediate mortality we have included all patients who died within one month of the onset of the attack and a few also who survived a week or two beyond this period but who continued gravely ill throughout all that time.

Levine's cases the immediate mortality in an attack was 53 per cent, but no statement is made as to the mortality in the first attack alone.

COMPARISON OF AGES OF THOSE WHO DIED IN THE FIRST ATTACK AND OF THOSE WHO MADE A GOOD RECOVERY

In order to determine if the age of the patient at the time of the first attack bore any important relation to the outcome of the attack, the age incidence, in five-year periods, of those who died in the first attack and of those who recovered and remained well for some time is

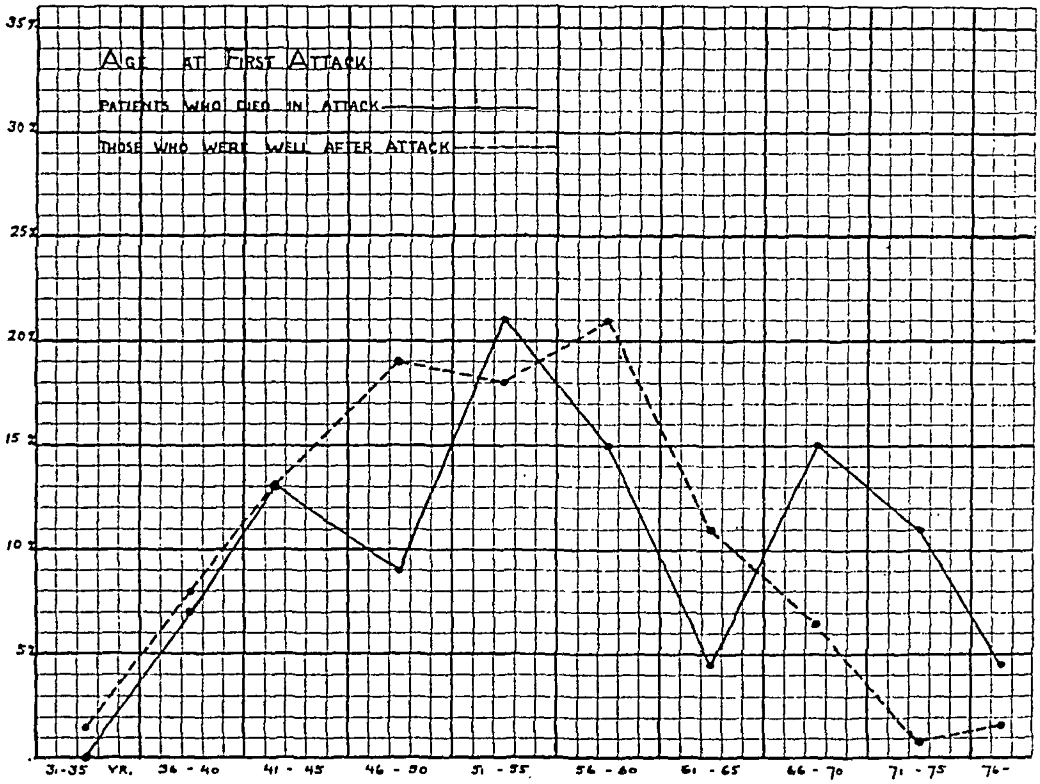

Fig. 6.

plotted separately in Fig. 6. It cannot be said that this comparison brings out any very convincing facts except that in the later age groups —from 66 years on—there is a disproportionately large percentage of the fatal cases and a small percentage of the patients who recovered and remained well.

RELATION OF THE IMMEDIATE PROGNOSIS TO THE SEVERITY OF THE SYMPTOMS OF THE ATTACK

In an effort to learn whether or not the outlook for immediate recovery from an attack bears any close relation to the intensity of the symptoms of the attack, all the cases (172) in which the data were sufficiently complete were divided arbitrarily into three groups, representing different degrees of severity of the initial symptoms of the attack. The criteria for this grouping, which necessarily is only a crude

one, were the intensity and the duration of the pain, the degree of dyspnea, and the severity of the shock—as indicated by the pallor, sweating, vomiting, fall of blood pressure and changes in the pulse. The results of this analysis are shown in Table I. It will be seen that

TABLE I

RELATION OF IMMEDIATE PROGNOSIS TO SEVERITY OF SYMPTOMS OF ATTACK (IN 172 CASES)

	DIED		RECOVERED	
Severity	Number	Per Cent	Number	Per Cent
+++	28	68	41	31
++	9	22	56	43
+	4	10	34	26
Total	41	100	131	100

among the fatal cases rather more than two-thirds had symptoms classed as very severe (+++), and only 10 per cent had symptoms classed as mild (+). On the other hand among the patients who recovered from the attack, 31 per cent had symptoms rated as very severe, and 26 per cent those rated as mild. In other words, although the immediate prognosis is certainly worse among patients having extremely severe initial symptoms, nevertheless almost one-third of those who recovered had symptoms of that character.

KNOWN DURATION OF PERIOD OF GOOD HEALTH AFTER FIRST ATTACK

Among patients who have made a good recovery from the first attack of coronary thrombosis, one of the very important points in prognosis is to know what may be considered to be their expectancy for good health. We have attempted to reach a rough approximation of such expectancy by tabulating the duration of good health in 89 patients who are still alive and well, and by including also 28 patients who are now dead but who were in good health up to the time of a second attack. As the patients of the first group are still alive and well, it is obvious that the figures derived from their records must be below the true ones for health expectancy. In the case of the second and much smaller group, however, the figures are of course accurate. As used by us the term "good health" indicates a state of health which permits the patient to live his accustomed life and to regard himself as essentially well. Not all were entirely free from pain or other discomforts, but these symptoms were not sufficient to cause the patient to modify his mode of life or to prevent him from working. Table II, which is

TABLE II

KNOWN DURATION OF PERIOD OF GOOD HEALTH AFTER FIRST ATTACK (89 PATIENTS ALIVE, 28 WELL UP TO SECOND ATTACK, DEAD)

3 MO.	6 MO.	1 YR.	2	3	4	5	6	7	8	9	10	11	12...17		
109	101	88	65	49	40	25	17	15	7	4	4	3	2	1	Patients (117)
93	86	75	56	42	34	21	15	13	6	3.4	3.4	2.6	1.7	0.9	Per cent

made up from the records of 117 patients, has been arranged to show the number of patients, and the percentage of the whole, who were in good health at the end of the different time periods. Thus at the end of three months after the first attack 109 (93 per cent) of the 117 were still well; at five years 17 (15 per cent); at ten years 4 (3.4 per cent), and finally at the end of 17 years one patient was still alive and well. This plan of tabulation has seemed to us to give a truer picture of the health expectancy than would be gained by merely recording the average duration of good health for the group.

FATE OF PATIENTS WITH ANTECEDENT CIRCULATORY SYMPTOMS

The relation between attacks of coronary thrombosis and an antecedent angina of effort has been so close that from the time of Heberden almost to the present time the clinical distinction between the two conditions has not been clearly recognized. Among the 274 patients of this series whose records were satisfactory upon this point, 105, or 38 per cent, had had antecedent anginal or other circulatory symptoms and 169, or 62 per cent, had had no such antecedent symptoms. In other words considerably more than half of all the patients had had no warning of any sort that would lead them to doubt the integrity of the heart.

In the group of cases presenting such antecedent circulatory symptoms the mortality in the first attack was 24 per cent, whereas that for all cases was 16.2 per cent. These facts appear in detailed form in Table III.

TABLE III

FATE OF PATIENTS WITH ANTECEDENT CIRCULATORY SYMPTOMS

169 Patients had no antecedent symptoms		62 per cent
105 Patients had antecedent symptoms		38 per cent
Angina of effort, few wk. to 10 yr.	64 cases	
Dyspnea on effort	24 "	
Angina and dyspnea	11 "	
Claudication	3 "	
Paroxysmal fibrillation	2 "	
Paroxysmal tachycardia	1 case	

Of these, 25 died in first attack, 24 per cent
(Against 16.2 per cent of all cases)

EFFECT OF ATTACK UPON ANGINAL PAIN

It has often been noted that occasional cases are seen in which troublesome anginal symptoms have ceased entirely after the successful ordeal of an attack of coronary thrombosis. In the group of patients having antecedent pain of a troublesome character and recovering satisfactorily from the first attack of coronary closure, there were 22 in whom this point could be satisfactorily investigated. In eight of the 22 patients anginal pain ceased with the attack of thrombosis and did not return. There were five patients in whom after the attack the pain

was worse than before. Two patients had less pain but were not entirely free, and in seven cases there was little or no change in the pain.

NUMBER OF ATTACKS

With respect to the number of distinct attacks of coronary thrombosis undergone, the 287 patients included in this series may be grouped as follows:

Single attack	190 patients	67 per cent
Two attacks	69 "	24 " "
Three attacks	12 "	4 " "
More than three attacks	14 "	5 " "
Doubtful	2 "	

It must be understood that these figures have *only* a limited significance, for they are derived not only from the records of 142 patients who are dead but also from those of 117 patients who are still living and from those of 28 patients who cannot now be traced. It is certain therefore that, among the patients living, fresh attacks will occur in many if not in most of them, and that the true percentages would differ from those given above by showing a smaller percentage of single-attack cases and a larger percentage of cases with a record of two or more attacks.

SINGLE-ATTACK CASES

Turning now to a study of the 190 patients who have had but a single attack, there were three who left the hospital as soon as the initial symptoms had subsided and of whom nothing further is known—not even whether or not they survived the first attack. The record of the other 187 cases may be summarized as follows:

Living and well	61	(33 per cent of 187)	50 per cent
Living but not well	27		
Fate unknown	11		
Died in attack	46	(16.2 per cent of 284)	50 per cent
Died after attack	42		

If this group of single-attack cases be further analyzed, with reference to those patients, both living and dead, who were *not* well after the attack, it is found that of 69 cases of that sort satisfactory data are available in sixty. These, together with the time interval since their attack, may be classified as follows:

Living, fair health	14	(2 months to 3 years; average 10 months)
Living, poor health	13	(2 months to 2 years; average 8 months)
Dead	33	(1 month to 3½ years; average 12 months)

The term "fair health" has been applied to those who had symptoms of a milder sort, such as anginal pain or dyspnea on effort, but who were able to lead a fairly normal life even though they were not well enough to work steadily. Most of the patients classed as having poor

health and as dead suffered from progressive cardiac failure. A few of those among the dead continued in fair health up to the time of their sudden death.

TWO-ATTACK CASES

The statistics of the 69 patients who had two attacks of coronary thrombosis are as follows:

Living and well after two attacks	15 or 22 per cent
Living but not well	5
Fate unknown	9
Died in second attack	20 or 29 per cent
Died after second attack	20

Comparison of these figures with those for the first attack reveals that whereas after the first attack 33 per cent of the patients were "living and well," after the second attack only 22 per cent could be so classified, and that whereas only 16.2 per cent of the patients died in the first attack 29 per cent died in the second.

INTERVAL BETWEEN FIRST AND SECOND ATTACKS

The interval of time which elapsed between the first and second attacks in 78 cases in which there were two or more attacks is shown in Table IV. In exactly half of the cases this interval was less than one

TABLE IV

INTERVAL BETWEEN FIRST AND SECOND ATTACKS (78 CASES)

UNDER 3 MO.	3-6 MO.	6-12 MO.	1-2 YR.	2-3 YR.	3-4 YR.	4-5 YR.	5-6 YR.	6-7 YR.	7-8 YR.	8-9 YR.	... 18 YR.	
20	6	13	11	7	3	3	7	2	4	1	1	Cases
	50 %											

year. Among the other half of the patients, however, the interval in many instances was very much longer and in one case was actually eighteen years.

THREE-ATTACK CASES

There were twelve patients who had three attacks of coronary closure. Of these, six (50 per cent) are still alive and well; two died in the third attack; three died after the attack and one patient was lost. In these patients the intervals between the first and second attacks varied from one month to seven years, and the intervals between the second and third attacks from one month to five years. In one patient these intervals were respectively five years and five years; in another patient, seven years and four years.

MULTIPLE-ATTACK CASES

Fourteen patients have had from four to seven distinct attacks of coronary thrombosis. Of these three are living (2½, 1¼, and 4½ years

after the first attack) and nine have died. The fate of two patients is unknown.

The patient who had seven attacks of coronary thrombosis was a physician who had his first attack at the age of 53 years and who died in the seventh at the age of 57. At the age of 42 years he had auricular fibrillation for several weeks following an appendectomy for acute suppurative appendicitis, and at the age of 45 years he again had auricular fibrillation, this time following an attack of influenza. Otherwise he had no cardiac symptoms until his first attack of coronary thrombosis in September, 1924. Subsequent attacks occurred in July, 1925, January, 1926, April, 1926, July, 1926, March, 1928, and June, 1928. These attacks were typical and severe and were accompanied by electrocardiographic changes. There was progressive diminution of cardiac reserve forcing a gradual restriction of activities. In November, 1927, there was an attack of nocturnal pulmonary edema, and four other attacks of pulmonary edema occurred during the following January and February.

VASCULAR COMPLICATIONS

Embolism.—Attacks diagnosed as those of embolism, in which presumably the emboli arose from mural thrombi in either the left or the right ventricle, were recorded 49 times among 42 of the 287 patients. Of these attacks 28 involved the systemic arteries and 21 the pulmonary artery. The details are as follows:

Cerebral	14
Renal	8
Mesenteric	3
Popliteal	1
Brachial	1
Retinal	1
	—
	28
Pulmonary artery	21

In two patients both systemic and pulmonary arteries were involved in the embolic attacks. Among the 42 patients concerned in the attacks of embolism, 27 recovered and 15 died—not necessarily, however, from the immediate effects of the embolic attack.

Thrombosis.—In considering the pathogenesis of coronary thrombosis the question often has been raised as to whether the chief determining cause was to be sought in the local arteriosclerotic process or rather in some constitutional thrombophilic tendency. In the records of the present series there is little to furnish support to the latter theory. Associated arterial thromboses are recorded in only two of the cases. In each of these there was the history of an antecedent cerebral attack, believed to be a thrombosis, and in each also a cerebral thrombosis many months after the attack of coronary thrombosis. In addition to these two cases of cerebral thrombosis there were four cases of venous throm-

bosis which manifested itself during or soon after the active symptoms of the cardiac attack. It seems probable that the advent of the venous thrombosis was determined rather by the sudden circulatory failure than by any constitutional tendency in that direction.

ELECTROCARDIOGRAMS

One hundred and fifty-one of the patients had one or more electrocardiograms; these are not all comparable, because in some cases the records were taken only at the time of the acute attack and in others only at some later time. The electrocardiographic changes were not on the whole a reliable aid in prognosis, but in general patients with normal or nearly normal records did best while those with evidence of arborization block or of bundle-branch block did badly. It is evident that if electrocardiograms are to be of real value in prognosis they must be taken at frequent intervals from the time of the attack onward, and that it is the progressive changes in the form of the tracing rather than its appearance at any one time that is significant.

TABLE V

ELECTROCARDIOGRAMS IN 151 PATIENTS

	PATIENTS	LIVING	DEAD	LOST
Normal or nearly normal records only	26	14	7	5
Changes in T-waves, with or without QRS change, not bundle-branch block	109	37	52	20
Heart-block, complete, 2:1 or dropped beats	7	4	2	1
Auricular fibrillation or flutter, transient or permanent	19	5	10	4
Bundle-branch block	15	4	10	1

SUMMARY

The records of 287 cases of coronary thrombosis have been studied with respect to the clinical course of the disease from the time of the first attack. Approximately 85 per cent of these cases were found in men and 15 per cent in women.

An analysis of the age incidence at the time of the first attack discloses the fact that in one-third of all the cases the first attack occurred before the fifty-first year, and in three-fourths of the cases before the sixty-first year. It seems evident therefore that coronary thrombosis must be regarded as essentially a disease of *early* middle life rather than of elderly life as it is usually held to be.

Evidence of an antecedent arterial hypertension was found in 34 per cent of the cases; of syphilis in 14 per cent, and of diabetes in 10 per cent.

Of the 287 patients studied 117 are known to be living and 142 to have died.

The immediate mortality in the first attack was 16.2 per cent.

Of 117 patients who recovered satisfactorily from the first attack, 75 per cent were in good health at the end of one year; 56 per cent at the end of two years; 21 per cent at five years and 3.4 per cent at ten years. One patient remained in good health for seventeen years and died in a second attack eighteen years after the first.

In 62 per cent of the patients the first attack supervened, without antecedent circulatory symptoms, in persons who had no reason to doubt the integrity of the heart.

A single attack only of thrombosis is recorded in 67 per cent of all the patients; two attacks occurred in 24 per cent; three attacks in 4 per cent and from four to seven attacks in 5 per cent.

Of the patients having but a single attack, one-half are living and one-third are in good health.

Among the patients having two or more attacks the time interval between the first and the second attack was less than one year in half of the cases and in the other half varied from one to eighteen years.

Signs of arterial embolism appeared 49 times among 42 patients. Twenty-eight of the embolic attacks involved the systemic arteries and 21 the pulmonary artery.

Although the immediate mortality in attacks of coronary thrombosis is higher when the initial symptoms are severe than when they are mild, yet almost one-third of the patients who recovered from the attack had symptoms of very severe character.

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THE EXCITATORY PROCESS OBSERVED IN THE EXPOSED HUMAN HEART*†

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INTRODUCTION

WHILE the general form of the electrocardiogram is the same for all vertebrates, even closely related mammalian species display curves which differ materially in detail. These differences, which are attributed to variations in the position of the heart with reference to the three standard leads and to peculiarities in the distribution of the ventricular conduction system, have led to considerable uncertainty in the application of the results of animal experiments to the interpretation of clinical electrocardiograms. For this reason studies of the human heart by means of a technique comparable to that employed in animal experiments are of great value. The opportunity to make a study of this kind upon an essentially normal human heart recently presented itself in the person of a young man upon whom a pericardiostomy was performed for suppurative pericarditis complicating a streptococcus pneumonia.

CASE SUMMARY

A white male, 30 years of age, entered the hospital Feb. 21, 1929, three days after the onset of lobar pneumonia of the lower lobe of the left lung. His past history revealed no symptoms referable to the heart. The physical examination showed the classic signs of pneumonic consolidation of the left lower lobe and revealed the heart to be normal in size and position, regular, rapid and free from any auscultatory signs of pathological change. The roentgenogram taken upon admission (Fig. 1) showed the heart to be normal in size, contour, and position, and also showed the consolidation of the lower lobe of the left lung. Electrocardiograms were usually normal, although at times the T-deflections were inverted in Leads II and III. Culture of the sputum showed streptococcus hemolyticus and streptococcus viridans to be the predominating organisms; pneumococci were not found. On Feb. 28, while the temperature was falling by lysis, a pericardial friction rub appeared and the temperature again rose. An effusion gradually developed and on March 9, a diagnostic puncture of the pericardium yielded sero-purulent fluid containing streptococcus viridans.

On March 12, an extrapleural pericardiostomy was performed under local anesthesia by Dr. John Alexander. The left fifth and sixth costal cartilages were removed, and an opening was made in the pericardium just to the left of the sternum

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from the fourth interspace to the diaphragm, measuring 6 by 4 cm. A considerable portion of the anterior, diaphragmatic and apical surfaces of the heart could be seen through this opening. Fig. 2 is a photograph of the wound made March 21. The opening remained for 21 days; it gradually became smaller so that on March 26, it measured 2.7 by 2.2 cm. The pericardium was irrigated frequently with Dakin's solution and later with 0.1 per cent mercurochrome solution, and the

Fig. 1.—Roentgenogram taken Feb. 21, 1929, showing the heart to be normal in size, contour, and position, and consolidation of the lower lobe of the left lung. The exposure was made with the patient lying on his back and with the tube at a distance of 3 feet.

Fig. 2.—Photograph showing the extrapleural pericardiostomy opening through which the heart was studied. The lower anterior surface of the right ventricle and the apex of the left ventricle may be seen. This photograph was made March 21, by which time the opening had become somewhat smaller than when most of the observations were made.

field was kept quite clean. On April 2, the opening was closed under nitrous oxide anesthesia. Up to this time the patient's condition had been good, but bronchopneumonia followed the anesthesia and the patient died on April 3.

The autopsy showed an early disseminated bronchopneumonia, and an older unresolved pneumonia of the left lower lobe. There were two small pockets of

encapsulated empyema, one just to the left of the upper thoracic spine and the other somewhat behind and to the left of the pericardium covering the left ventricle. The heart was normal in size and position and was covered by an organizing fibrinous exudate, but there was no gross abnormality of the musculature, valves, or internal architecture. Microscopically there was subendocardial fatty degenerative infiltration, slight atrophy of the myocardium, cloudy swelling, and early Zenker's necrosis.

The clinical, electrocardiographic, roentgenological, and post-mortem findings indicate, therefore, that for the purpose of the experiments presently to be described the heart was essentially normal in all respects, and that the results of studies made upon it may be applied without reservation to the interpretation of the human electrocardiogram.

When the exposed heart is experimented upon in a human subject only those procedures are justified which can be expeditiously carried out and which entail no great danger or inconvenience to the patient. Two sets of observations which met these requirements and which promised results of value were carried out. The first section of this article is devoted to the normal spread of the excitatory process studied by means of direct electrocardiographic leads from various points upon the ventricles taken simultaneously with standard Lead II. The second section is concerned with the analysis of the curves obtained by electrical stimulation of a series of points on the right and left ventricular surface, and with the bearing of these curves upon the interpretation of clinical electrocardiograms depicting ventricular extrasystoles, bundle-branch block and ventricular preponderance.

I. THE NORMAL SPREAD OF THE EXCITATORY PROCESS IN THE VENTRICLES

METHODS—

1. *Electrical Arrangements.*—The method used for studying the order in which various points on the surface of the ventricles became active was essentially that of Lewis and Rothschild[15] in observing this process in the dog. Only their second method in which they employed a single contact on the heart paired with a fixed distal electrode, usually attached to the chest wall, was used in our experiments. It was, however, necessary to make certain modifications of their technique. In the first place, as the heart was not completely exposed it was necessary that the electrode for exploring the ventricular surface be flexible, and since the subject was human, that it be sterilizable.

For this purpose an electrode was devised utilizing the principle described by Adrian[1] whereby a nonpolarizable electrode was obtained by immersing a silver wire coated with electrolytically deposited silver chloride in a solution of sodium chloride. The general construction of this electrode is shown diagrammatically in Fig. 3. This instrument was flexible enough to be bent into whatever shape was necessary, but stiff enough to withstand without bending whatever pressure was necessary to make a satisfactory contact with the ventricle. Sterilization was accomplished by boiling it in strong saline and during the experiment the tip was frequently moistened and cleansed with this solution. The electrode seemed entirely free from polarization effects and though the tip was not so small as that of the instrument used by Lewis and Rothschild, yet, since it was not possible to locate points so accurately as they did, a smaller tip would not have appreciably increased the accuracy of the results so far as nicety of location was concerned.

Since the patient's condition was such that it was deemed unwise to bring him to the laboratory all observations were made over the hospital electrocardiographic distribution system. This limited the number of lead wires with which to obtain two simultaneous records to three. Consequently it was necessary to use the ordinary lead-off from the left leg as the distal contact to be paired with the direct contact and to attach the special electrode to the wire usually employed as lead-off from the left arm. The proper arrangements were then made in the laboratory to obtain ordinary Lead II and the direct lead, special electrode-left leg, simultaneously. The records were taken with two Einthoven galvanometers optically coupled in tandem so that the images of both strings are projected upon the camera in a single homogeneously illuminated optical field. Records were thus obtained whereby it was possible to time the electrical events taking place at that point on the surface of the heart upon which the special electrode had been placed with reference to those of standard Lead II.

2. *Location of points.*—Obviously in an experiment such as this, accurate localization of the points studied was of the utmost importance. To this end an outline drawing of a normal human heart was prepared and the points from which records

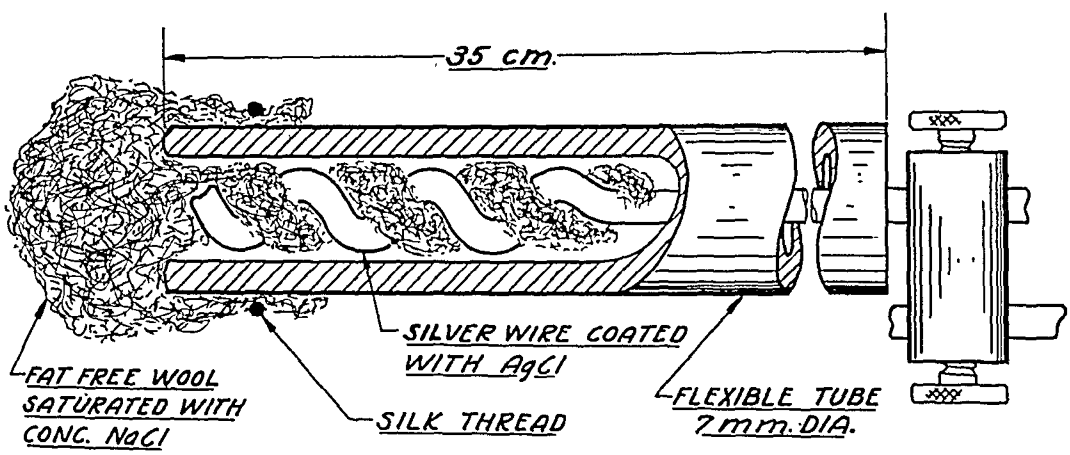

Fig. 3.—Diagram of the electrode used for leading directly from the heart. The flexible rubber tube contains the silver wire, coated with silver chloride and coiled with wool saturated with sodium chloride.

were desired were marked upon it. A few of these points were visible through the wound, *h* and *g* (Fig. 5), *4* and *6* (Fig. 7) and others were just under the edge of the wound *5* and *3* (Fig. 7), *e* and *k* (Fig. 5). The remaining points were located as follows. The surgeon noted the position of these points on the chart with reference to the visible points and with reference to the borders of the heart shown in the outline drawing. He then laid the electrode upon the surface of the chest and measured the distance from the edge of the wound to the surface landmark; rib, interspace, sternal edge as the case might be, which he estimated to lie immediately over the point desired. The electrode was then introduced beneath the edge of the wound for the measured distance and in the proper direction. In each instance the electrode was held steady while the record was being taken. The records were numbered to correspond with the numbers on the chart. This was easily accomplished as the laboratory and the patient's room were in constant telephonic connection during the experiment. Finally, when the heart was obtained at autopsy all notes were consulted and each point located as accurately as possible. It should be mentioned that the anatomical landmarks on the heart itself could be much more easily recognized at the time of the experiment than at the time of autopsy. At the time of the experiments, there was visible on the surface of the heart at the left margin of the wound a strip of edematous fat, which, as was ascertained post-mortem, lay in the interventricular groove. By lifting the tissue at

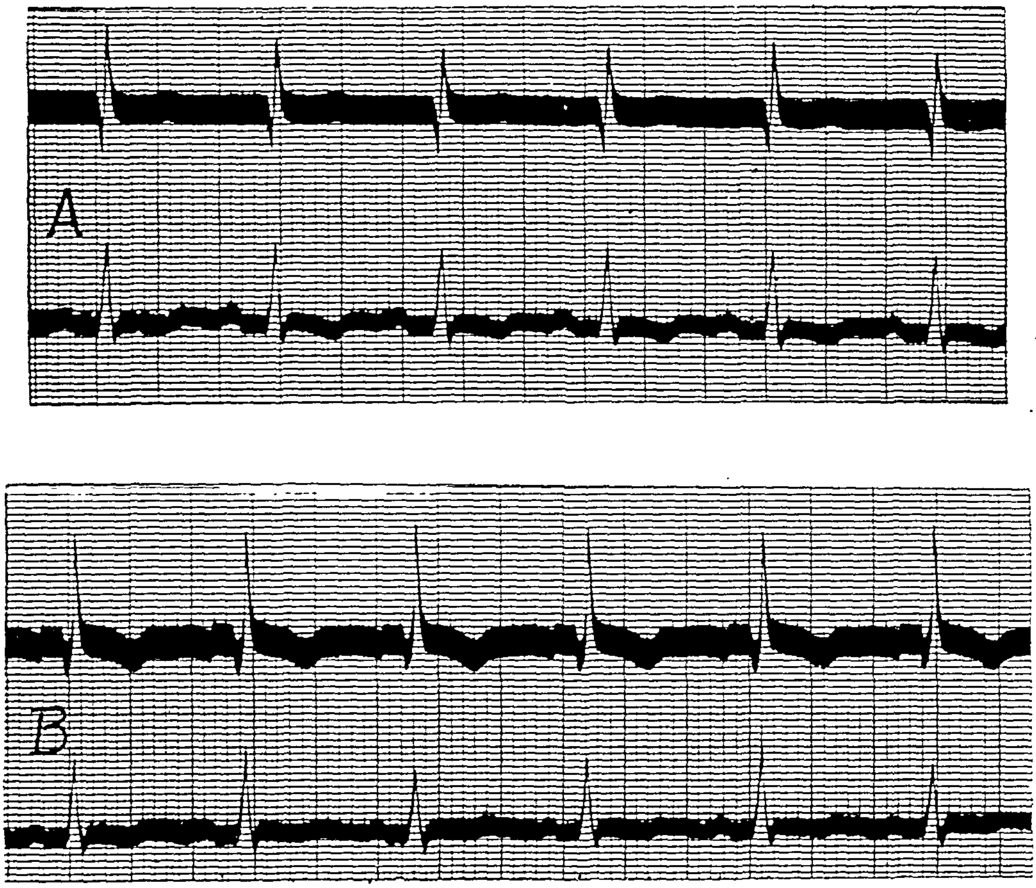

Fig. 4.—Curves showing a direct lead (upper) and standard Lead II (lower) taken simultaneously. In *A* the direct lead is from the conus arteriosis (Fig. 5, point *a*); the intrinsic deflection begins .0143 sec. after the beginning of R of Lead II. In *B* the direct lead is from the postero-lateral surface of the left ventricle very near the A-V groove (Fig. 5, point *l*). The ventricular intrinsic deflection begins .0229 sec. after the beginning of R of Lead II.

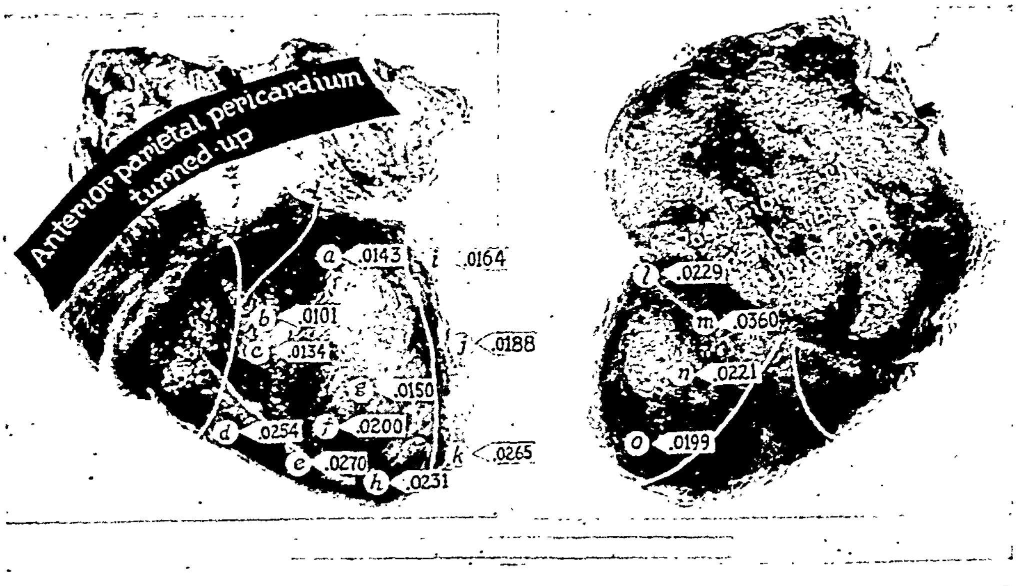

Fig. 5.—Photographs of the heart showing the points from which direct leads were taken and the times after the beginning of R of Lead II at which activity arrived at these points. The white lines mark the interventricular groove, auriculo-ventricular junction, and junction of aorta and conus arteriosus. Points *a*, *i*, and *k* were tested on March 23 and again on March 24, *c* and *f* on March 24, the remaining points on March 23.

the margin of the wound and peering beneath it the apex of the left and a considerable part of the diaphragmatic surface of the right ventricle not directly visible through the wound could be seen.

When the heart was examined post-mortem it was possible to identify the exposed points and those which lay just beneath the margin of the wound with a high degree of accuracy. Regarding the points farthest from the wound, particularly those on the posterior surface of the heart, greater uncertainty exists; but there can be no doubt as to their approximate location.

RESULTS—

All of the curves obtained by direct leads from points on the surface of the ventricles are similar to those described by Lewis and Rothschild.[15] The deflections resemble those of the ordinary electrocardiogram in a general way except that, as a rule, no P-deflections can be made out (Fig. 4). Two elements in the QRS complex are recognizable, a relatively slow deflection, usually directed downward, interrupted by a quick upward deflection of relatively great amplitude, following which the string more slowly returns to the neutral position. This large quick deflection was shown by Lewis and Rothschild to be caused by activity of the muscle directly beneath the electrode and was referred to by them as the intrinsic deflection, all others being called extrinsic. Extrinsic deflections are caused by activity in the muscle elsewhere than beneath the electrode. The intrinsic deflection is recognized by the following characteristics: it is, in any given experiment, always in the same direction (upward in this present one), of large amplitude and short duration; furthermore, the time of its occurrence relative to the beginning of R in Lead II is not altered by changing the position of the distal electrode, even though this procedure greatly modifies the appearance of the complex as a whole. The time after the beginning of R in Lead II at which each of the various points studied on the surface of the ventricle became active was determined, as in the experiment of Lewis and Rothschild, by measuring the time interval from the beginning of the R-wave in Lead II to the beginning of the intrinsic deflection. These time intervals and the locations of the respective points are shown in Fig. 5. The figures represent the average of a number of determinations. The individual measurements varied by less than .001 sec. From a number of points two sets of records were taken, one using the left leg as the distal electrode and one using the right arm. The greatest variation between the times at which the intrinsic deflections occurred in two such records was .002 sec., and in this case the electrode may have moved slightly during the time consumed in making the necessary readjustments for taking the second record. When the same points were studied on different days there was close agreement between the results. As a typical example, the time of arrival of activity at point *a* was on March 23, .0143 sec. and on March 24, .0140 sec. after the beginning of R in Lead II. The Lucas Comparator was used in all cases to measure the records.

The earliest point to become active was *b*, high on the anterior surface of the right ventricle near the tip of the right auricular appendage. This point showed negativity .0101 sec. after the beginning of R in Lead II.

Other early points on the right ventricle were on the conus arteriosus, *a*, and on the anterior surface near the base of the large papillary muscle, *g*; these points became active .0143 and .0150 sec. respectively, after the beginning of R in Lead II. The earliest points on the left ventricle were high on the antero-lateral surface near the left auricular appendage (*i*), and on the left apex posteriorly (*o*); the figures for these points were .0164 and .0199 sec. respectively. The latest point was on the posterior surface of the left ventricle near the atrio-ventricular groove (*m*); it became active .0360 sec. after the beginning of R in Lead II.

DISCUSSION

The order in which the various points on the surface of the ventricles became active differs in some respects from that found by Lewis and Rothschild[15] in the dog. It will be noted that the earliest points discovered (*b* and *c*) were on the anterior surface of the right ventricle near the atrio-ventricular groove and just inferior to the area where the aorta presents anteriorly. Lewis and Rothschild consistently found the earliest region to become active to be on the anterior surface of the right ventricle near the base of the large papillary muscle, a region corresponding to point *g*, Fig. 5. The difference between their results and ours may be accounted for in a number of ways. It may be the result of a technical error in our experiment. This seems improbable, however, because the readings from points *b* and *c*, which are in close agreement, were obtained on different days, and the results were checked by changing the position of the electrode which was paired with the direct lead. Furthermore, the figures for these points are supported by the early reading from point *a* at the base of the conus arteriosus, which was also checked. This region is relatively late in the dog. It would seem, therefore, that some anatomical explanation for the early arrival of the excitation process at the atrio-ventricular border must be sought. The right atrio-ventricular bundle described by Kent[11] comes to mind, but these results, while consistent with Kent's findings, cannot in the present state of our knowledge be considered evidence for them. Finally, it is possible that the right division of the His-bundle branches earlier than has usually been assumed. No evidence of early branching, or bridging, could be discerned, however, upon gross examination of the heart, and careful study by special methods of the distribution of the conduction tracts was not possible in this case. Differences in the thickness of the ventricular muscle at the points studied cannot be held to account for the

early arrival of excitation at points near the atrio-ventricular groove, because the muscle was thicker at these points than at other relatively early points.

II. THE CURVES PRODUCED BY ELECTRICAL STIMULATION OF THE VENTRICLES

METHODS—

In previous studies of artificially induced extrasystoles in man, mechanical stimulation of the heart has been employed almost exclusively. In the patient studied by the present authors, however neither pricking, pinching nor tapping the ventricles induced premature beats, except infrequently. Electrical stimulation was therefore resorted to. An ordinary Du Bois-Reymond inductorium adjusted to deliver single shocks was used. The secondary was adjusted by trial to deliver stimuli of approximately threshold value, which for most of the regions studied were of about 30 volts.

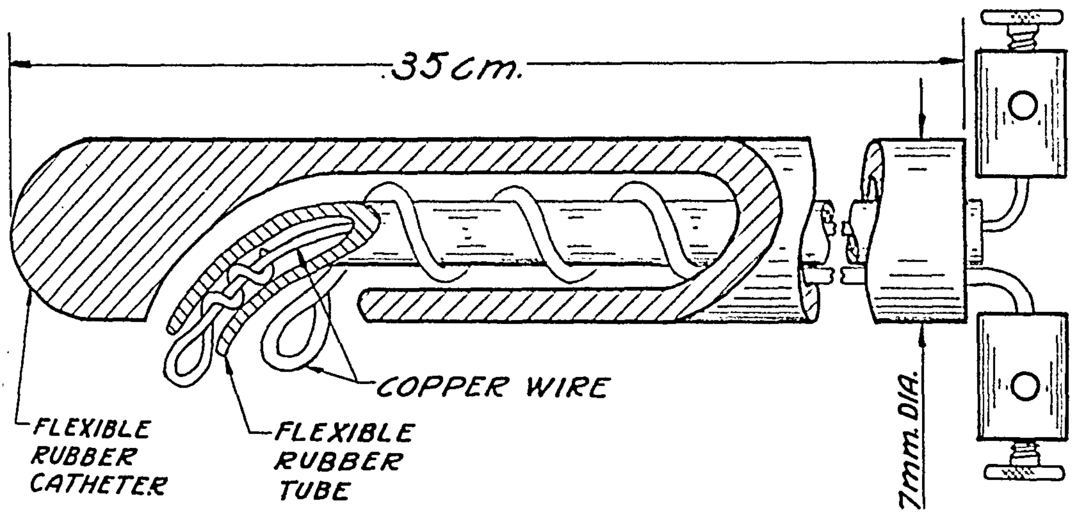

Fig. 6.—Diagram of the stimulating electrode.

As in the case of the non-polarizable electrode already described it was necessary that the stimulating electrode be both flexible and sterilizable. Its general construction is shown in the diagram (Fig. 6). Particular care was taken that the smooth contact points, which were about 3 mm. apart, did not project far beyond the eye of the catheter.

Simultaneous records were obtained according to the method of Einthoven, Bergansius and Bijtel.[4] Lead I was recorded by a large Hindle and Leads II and III by the two Einthoven galvanometers previously referred to. For locating the points stimulated and identifying the records from these points the same method was used as described for the location of points from which direct leads were obtained.

RESULTS—

The electrocardiograms of the premature ventricular contractions induced by electrical stimulation of the ventricles and the locations of the points stimulated are shown in Figs. 7 and 8. These electrocardiograms resemble the clinical records of ventricular extrasystoles. The deflections are essentially diphasic in Leads I and III, in that the T-wave has a direction opposite to the chief initial deflection. The

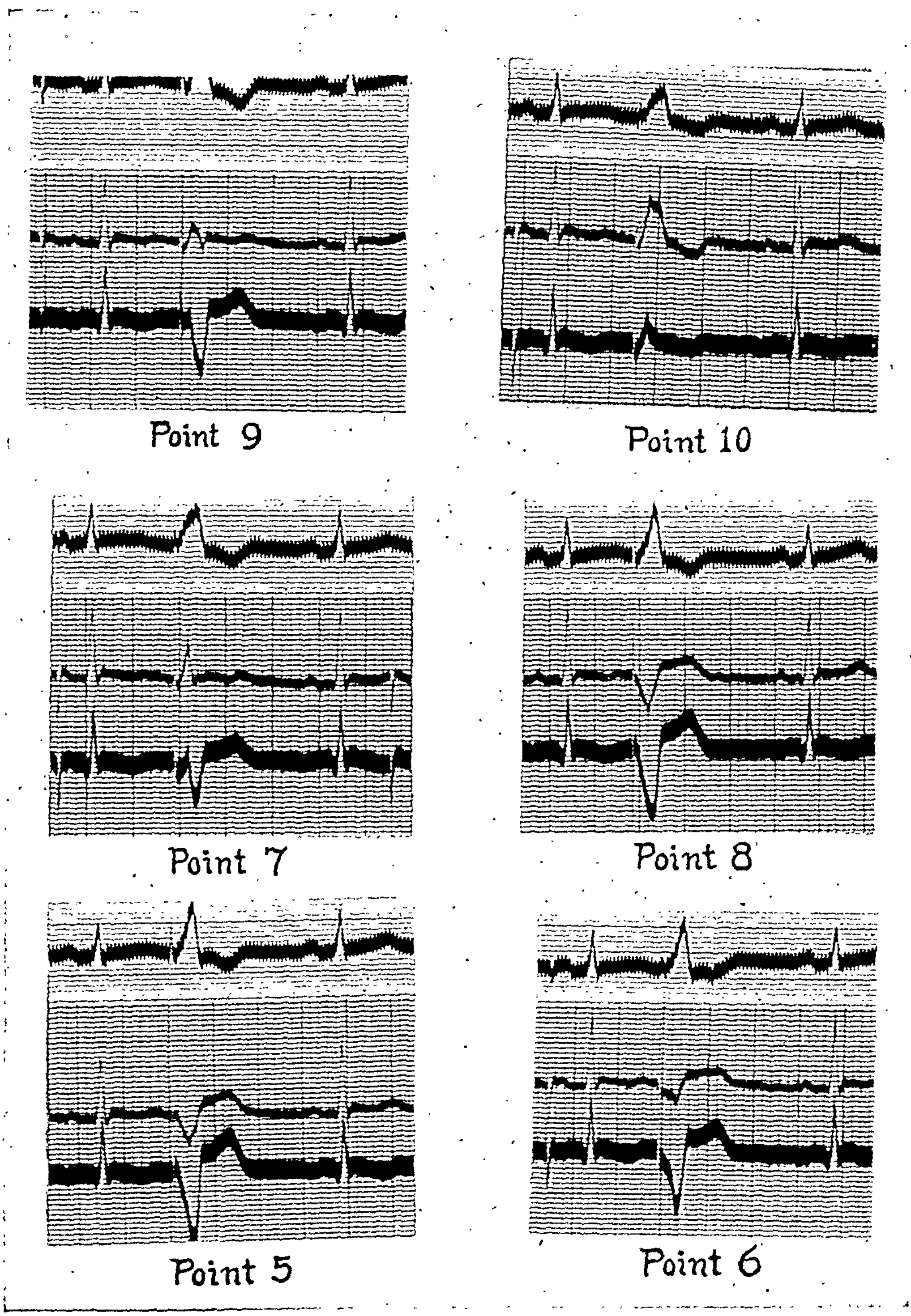

Fig. 7A.

Fig. 7.—Electrocardiograms of the three standard leads taken simultaneously showing the ventricular premature beats induced by direct electrical stimulation of the points indicated on the anterior aspect of the heart on March 19. *The forced* contractions are preceded by sharp deflections produced by the stimulating current. When the stimulating current fell in the refractory period these sharp deflections are not followed by ventricular complexes. Points *2*, *3*, *4* and *5* were also tested on March 18. *Point 1* was tested again on March 24. The top curve is Lead I, the bottom, Lead III.

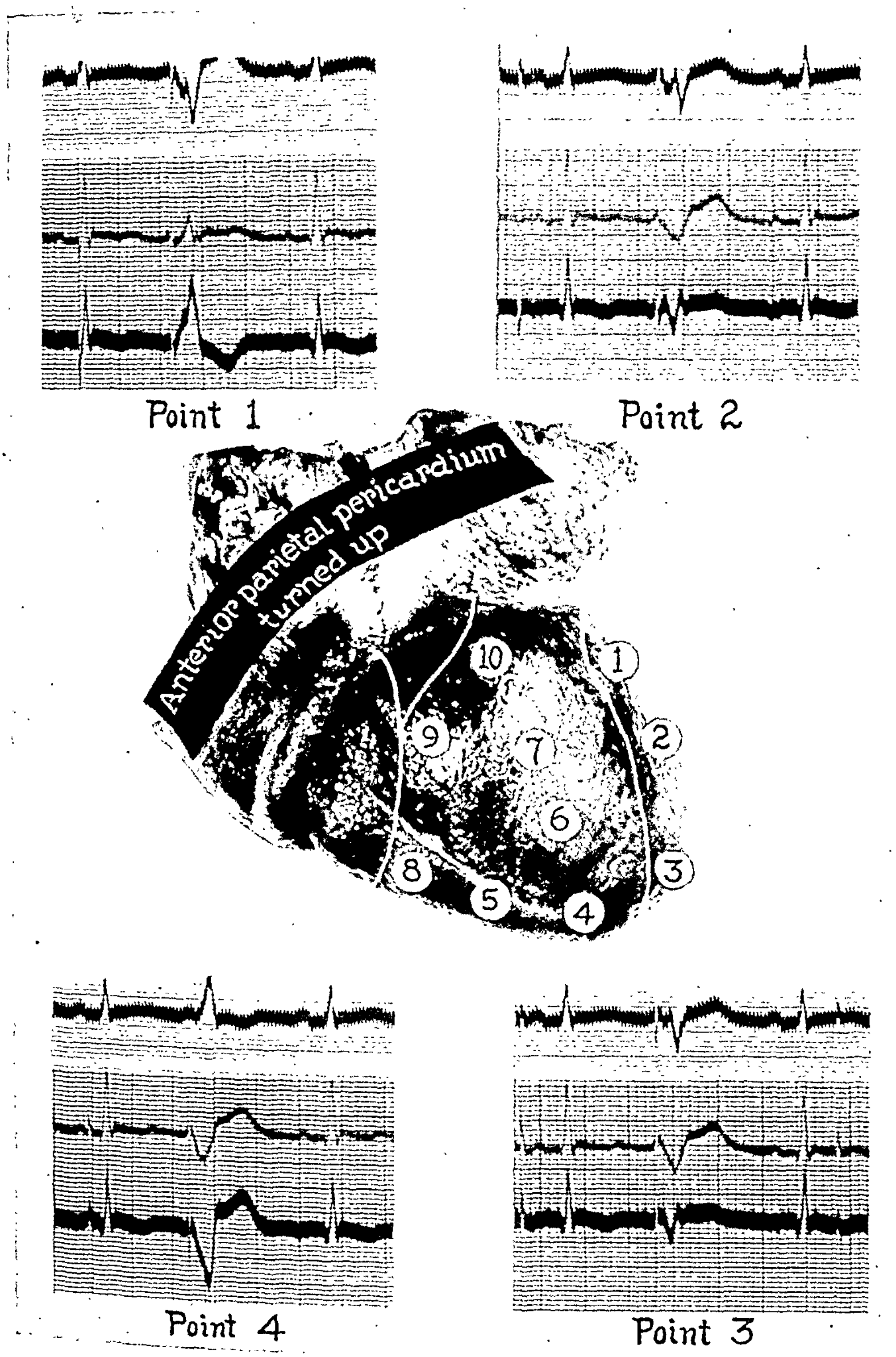
Point 1
Point 2
Anterior parietal pericardium turned up
10
1
9
7
2
6
8
3
5
4
Point 4
Point 3

Fig. 7B.

QRS interval is much greater than the QRS interval of the normal complexes. These forced contractions may be grouped into four main types: (1) those arising from most of the anterior surface of the right ventricle, which show chief initial deflections that are upward in Lead I and downward in Lead III (points *4, 5, 6, 7, 8, 9*); (2) those arising from the right ventricle in the region of the conus arteriosus, which show chief initial deflections that are upward in all three leads (point *10*); (3) those arising from a point high on the antero-lateral surface of the left ventricle near the left auricular appendage, which show initial deflections that are downward in Lead I and upward in Lead III (point *1*); and (4) those arising from all other points on the surface of the left ventricle, which show chief initial deflections that are downward in all three leads (points *2, 3, 11, 12*). Thus, it is seen that in Lead I all of the chief initial deflections from the right ventricle are upward and all from the left ventricle downward, while in Lead III those arising from the conus and an adjacent area high on the left ventricle are upward and those from all other parts of the heart, including its apical portion, are downward. The deflections in Lead II usually, but by no means always resemble those of Lead III. In Lead II the chief initial deflections are upward in the beats arising from points on the anterior surface of right and left ventricles near the cephalic aspect of the heart and downward in beats arising from all other points.

DISCUSSION

1. *Ventricular Extrasystoles.*—An experiment such as has just been described might reasonably be expected to answer several questions. First to mind, perhaps, is whether there is any constant characteristic of the curves of premature ventricular contractions which is dependent upon the ventricle from which they arise, or whether the form of such curves is simply determined by the position of their point of origin relative to the base or apex and to the right or left border of the heart quite independently of its relation to the ventricular septum. If points of approximately the same level in the two ventricles are compared (Fig. 7), point *10* with *1*, *7* with *2*, *4* with *3*, it will be seen at once that in all curves from the right ventricle the chief initial deflection is upward in Lead I and in those from the left ventricle it is consistently downward in this lead. That this change in form is attributable to crossing the interventricular septum and not simply to a change in position from right to left can be seen by noting the close similarity between the curves obtained from points *8* and *6* (Fig. 7). These points are much farther apart than any of those previously compared, but are both on the same ventricle at approximately the same distance from the inferior border of the heart. It would seem therefore that when the Purkinje system of the right ventricle is excited in advance of that of the left, an upward deflection occurs in Lead I, and

Fig. 8.—Electrocardiograms of the three standard leads taken simultaneously showing the ventricular premature beats induced by direct electrical stimulation of the points indicated on the posterior aspect of the heart on March 19. The top curve is Lead I; the bottom, Lead III.

when the left Purkinje system is excited earlier than the right a downward deflection is produced in this lead.

The position of the point first excited relative to the cephalic and caudal aspects of the heart is, however, not without its effect. As the cephalic aspect of the heart is approached there is a tendency for the chief initial deflection of Leads II and III to become upright, whereas in the more caudal regions this deflection tends to be inverted. On the right ventricle this is best shown in Lead II. If attention be directed to points *10*, *7*, *6*, and *4* (Fig. 7), which are arranged in approximately a straight line from conus to apex, it will be noted that in Lead III the chief initial deflection is upright at point *10* and inverted in all of the other locations, that in Lead II it is upright and of large amplitude at *10*, still upright but of smaller amplitude at *7*, slightly inverted at *6*, and definitely inverted at *4*. This tendency of the chief initial deflection to become more and more inverted as the lower portion of the ventricles is approached is more striking and orderly if reference is made to the cephalic and caudal aspects of the heart as it lies in the body rather than to the apex and base. For example points *8*, *9*, and *10* are all on the basal portion of the right ventricle, but are one above the other with reference to the long axis of the body and it is upon this latter arrangement apparently that the change in the form of the curves obtained from them depends. This change in the form of Leads II and III with the point stimulated is probably caused by the altered order in which various portions of the ventricle become active, or in other words by the altered spread of the impulse through the subendocardial Purkinje plexus, right or left, which it enters first and perhaps to a slight extent by variations in its course through the plexus of the opposite side. This phenomenon is more pronounced in our curves from the right ventricle than in those from the left; the remarkable similarity between the curves obtained from points *2* and *3* leads us to suspect, however, that point *2* was actually closer to point *3* than our chart would indicate. If this is the case the difference between the two ventricles with respect to the phenomenon in question may be more apparent than real.

These observations show that the form of the electrocardiogram of a forced ventricular contraction is dependent not only upon the Purkinje system, right or left, to which the impulse first spreads, but also upon the level with reference to the long axis of the body at which it enters this system. Lead I indicates the former, and leads II and III the latter.

Curves of the type which Lewis[12] has called concordant (main initial ventricular deflections in the same direction in all three leads) and discordant (main deflections not all in the same direction) are obtained from both ventricles. The concordant graphs obtained from the right ventricle (point *10*, Fig. 7) have upward initial ventricular

deflections and those from the left ventricle, inverted. This is entirely in accord with the accepted view of the subject. The discordant curves, on the other hand, are not in agreement with current electrocardiographic interpretation. In fact, the curves obtained from the right ventricle are of the type which, when naturally occurring, have hitherto been thought to be of left ventricular origin, whereas, the discordant curves obtained from the left ventricle are of the type previously believed to originate in the right ventricle.

The generally accepted view regarding the origin of ventricular extrasystoles represented in the electrocardiogram by curves of the discordant type, with which, as we have pointed out, our results are not in agreement, is derived almost entirely from the current interpretation of clinical electrocardiograms depicting bundle-branch block. As we shall have occasion to discuss this matter in a later section of this article we may omit further consideration of it here.

Our results are similar in a broad sense to those which have been obtained in animals by other investigators. Most of the work on animals, however, was done many years ago and, except in a few instances, only a single lead was employed. For the sake of brevity we shall describe here only the comprehensive investigation of this subject reported by Rothberger and Winterberg[18] in 1913. They employed Lead I and an anus-oesophagus lead. The curves which they obtained from the dog's left ventricle closely resemble those recorded by us from similar locations on the human left ventricle with one exception. They found a small region in the anterior surface of the left ventricle close to the septum which gave discordant curves in which the chief initial deflection was upward in Lead I and downward in the anus-oesophagus lead; no curves of this type were obtained by us from the left ventricle. The curves which they obtained from the dog's right ventricle differ materially from our human curves from this chamber. In their experiments all of the anterior surface of the right ventricle and a narrow basal strip on the posterior surface gave concordant curves in which the chief initial deflection was upright in all leads, whereas in our experiments concordant curves of this type were obtained from a small region on the conus only. From the remainder of the posterior surface of the right ventricle they obtained discordant responses, similar to those which we recorded from the anterior surface of this chamber in man. Rothberger and Winterberg point out at the end of their article that the application of their results to human pathology is not permissible. The wisdom of this reservation is apparent when their curves are compared with those which we have obtained in man, and yet a broad similarity exists.

The present authors were able to find in the literature only four attempts to obtain electrocardiograms of artificially induced extrasystoles in man. The first was that of Hoffmann.[9] His published re-

port, however, does not contain sufficient data to make an evaluation of his results possible. Recently an article appeared by Fossier[7] who induced extrasystoles in a patient who had a congenital deformity of the sternum and in whom the heart was covered by skin and soft tissue only. The heart was stimulated by striking the precordium with a percussion hammer and the three standard leads were taken in rotation. The author interpreted his results as indicating that the form of the forced contractions depended, not upon the ventricle from which they arose, but upon the position of their points of origin relative to the base or apex of the heart. It is probable, however, that the location of the points stimulated was not as accurate as the author believed. It would require only slight reinterpretation of the locations of these points to bring his results into agreement with those here reported.

The most important previous attempt to obtain extrasystoles from known locations on the human ventricles was that of Oppenheimer and Stewart.[17] These investigators studied a patient who had had a resection of all the ribs on the left side excepting the first. The costal cartilages however remained. This left a part of the heart covered solely by the skin. The three standard leads were obtained simultaneously and the heart was stimulated by striking it with a percussion hammer. As the authors interpreted their results they believed them to be in harmony with the generally accepted view. Since the heart was displaced to the right, we suggest however that the approach to the heart in their patient permitted them to reach the left ventricle only, a possibility which they discuss in their article.

If it be admitted that the extrasystoles which Oppenheimer and Stewart obtained resulted from stimulation of various points on the left ventricle, their results are not in conflict with those here reported. Under these circumstances the curves which show downward chief deflections in Lead I and upward deflections in Lead III, which they obtained near the auriculo-ventricular junction, correspond to the curves obtained from point *1* (Fig. 7) in this study, and those in which the initial deflections are downward in all three leads, which they obtained from more apical regions correspond to the curves from points *2* and *3* (Fig. 7) and points *11* and *12* (Fig. 8).

Oppenheimer and Stewart also publish a curve which Prof. Einthoven obtained when he stimulated what he believed to be the right ventricle. His patient had had a portion of the sternum and several ribs removed at an operation subsequent to an accident. Einthoven refers to this experiment and publishes the curve in his Nobel lecture,[5] but gives no further details. The curve is of the type obtained by us from point *1*.

Considering the unavoidable inaccuracy in locating the point stimulated when the heart, covered by the skin and subcutaneous tissues,

is stimulated mechanically by striking the precordium, it is obvious that our results are not in conflict with any previous observations reported in the literature. It is apparent also that the current view regarding the site of origin of extrasystoles represented in clinical electrocardiograms by curves of the discordant type are not based upon satisfactory direct observations in man nor upon direct observations in animals, but upon inference. Admitting that forced contractions produced by electrical stimulation of the epicardial surface of the ventricles are not necessarily comparable in all respects to extrasystoles of spontaneous origin, which are widely held to arise within the special tissues, we suggest that this view should be revised in accordance with the evidence which we have presented.

2. *Bundle-Branch Block.*—The observations which we have described were planned and carried out with the hope of obtaining information bearing upon the interpretation of human branch block and preponderance curves. This hope was founded upon the belief, which is widely expressed and implied in the literature, that the ventricular complexes produced by stimulating the right or left ventricle and those produced by cutting the opposite branch of the His-bundle are similar in form. This belief is derived both from observation and from theoretical considerations.

When one branch of the His-bundle is cut, an impulse which descends from the auricles passes down the intact branch and spreads through the subendocardial Purkinje plexus of the contralateral ventricle and outward through its walls exactly as before. It does not reach the subendocardial plexus of the homolateral ventricle until it has pierced the septum and the activation of this chamber is considerably delayed.

As Lewis[14] and Wilson and Herrmann[20] have pointed out, the course of the excitation wave set up when one ventricle is stimulated electrically is in many respects similar. From the point of stimulation the excitation process spreads in all directions with the slow speed characteristic of conduction in ventricular muscle. As soon as it reaches the subendocardial plexus, however, it spreads with great rapidity over the entire endocardial surface of the ventricle stimulated. The activation of the muscle of the other ventricle is delayed to the same, or nearly the same, extent as in bundle-branch block.

In both cases, therefore, the muscle of one ventricle is activated considerably in advance of the muscle of the other, and in both cases the excitation process spreads with great rapidity over the endocardial surface of this ventricle and traverses its walls from within outward. The course taken by the excitation wave through the subendocardial Purkinje plexus of this ventricle will differ in the two cases, but to what extent will depend upon the location of the point stimulated upon the surface of the heart. If the forced excitation wave enters the

Purkinje plexus in a region that is one of the first to which the natural impulse spreads, the difference will probably be slight; if it enters this plexus in a region which is naturally a late one, the difference may be considerable.

The form of the ventricular complex is determined by the direction and order in which the ventricular muscle passes into the active state, and the considerations outlined above indicate that the ventricular complexes produced by cutting one branch of the His-bundle and those produced by stimulating the opposite ventricle will be similar, but that the degree of similarity will depend to a considerable extent upon the point stimulated.

In describing an experiment in which the effect of stimulating a series of points on the anterior surface of the dog's heart were recorded in Lead II, Lewis[13] called attention to the similarity between the responses obtained from the right and left ventricles and the complexes produced by cutting the opposite bundle in each case. He pointed out that when the usual leads and usual string sensitivity were employed, stimulation of the ventricular surface produced little or no movement of the galvanometer string until the Purkinje plexus was involved. The theoretical considerations, essentially those outlined above, which he puts forward to explain the similarity of the curves obtained by stimulation of a large area of the right or left ventricle apply with equal force to the resemblance between right or left ventricular responses and left or right branch block curves respectively.

Wilson and Herrmann[20] showed that in many instances stimulation of the right central region in the dog produced complexes, not merely similar, but practically identical in the single lead employed, with the complexes obtained by cutting the left branch of the His-bundle. They demonstrated also that when right branch block was present, stimulation of the right central region at the proper instant in late diastole, so that the forced excitation wave reached the terminals of the right branch of the His-bundle at the same instant that the natural impulse reached the terminals of the left branch, resulted in a complex hardly distinguishable from the normal complexes of the same animal. When the right branch block complex and the forced complex were charted and added algebraically in the proper time relations the same result was obtained. They point out that the point stimulated in this instance lay approximately over the point where the right branch of the His-bundle breaks into its arborization. Assuming that this branch gives off no important subdivisions at a higher level, the reason for the similarity between the forced complexes and those obtained by cutting the left branch of the His-bundle are obvious.

Although in the experiments referred to only a single lead was employed the theoretical considerations apply to all three leads with

equal force.* Furthermore the similarity in question is not merely a general one, but often extends, at least in single leads, to the minor details.

On the other hand it is obvious that stimulation of all points on the right or left ventricle does not necessarily give complexes bearing a close resemblance in all leads to those produced by cutting the opposite branch of the His-bundle. In the dog and in man both concordant and discordant curves are obtained from both ventricles. In the dog the chief initial deflection is upright in all leads in left branch block and inverted in all leads, except in rare instances, in right branch block. Stimulation of the anterior surface of the right ventricle, including the region overlying the anterior papillary muscle where the right branch of the His-bundle breaks into its arborization, produces complexes which resemble left branch block complexes in all leads. Stimulation of a considerable portion of the posterior surface produces curves which resemble left branch block curves in Lead I only. Stimulation of the larger part of the surface of the left ventricle also produces curves which resemble those obtained by cutting the opposite branch of the bundle in all leads. There is a small region near the septum at the apex which gives curves which resemble right branch block curves in Lead III only, and another small region at the base which gives responses which resemble right branch block curves in Lead I only. No point on either ventricle gives complexes which resemble those produced by cutting the bundle branch on the same side in all leads, or differ from those produced by cutting the opposite bundle branch in all leads.

When the complexes obtained by stimulation of the human ventricles are examined with these facts and considerations in mind, it will be seen that they are in apparent conflict with the current interpretation of clinical bundle-branch block curves.

The curves obtained by stimulation of the anterior surface of the right ventricle, except a small region on the conus, closely resemble in all leads the curves which are at present ascribed to right branch block. There are three possibilities to be considered.

1). The curves obtained by stimulation of the anterior surface of the right ventricle, including the central region and other points which are naturally activated early, resemble the curves produced by cutting the opposite bundle branch *in all leads,* as they do in the dog.

2). These curves resemble the curves produced by lesions of the bundle branch on the same side *in all leads,* but do not resemble the curves produced by lesions of the opposite bundle branch *in any lead.*

3). The resemblance in question is accidental and without significance.

*With the help of Dr. Wilson we have repeated the experiments which he did with Herrmann, recording Leads I and III simultaneously. The results were identical.

Of these possibilities only the first appears to us acceptable, and we suggest for this reason that the electrocardiograms now regarded as indicating right branch block in man are in reality due to left branch block and *vice versa*.*

In the case of the left ventricle, the conflict between our results and the current view of bundle-branch block in man is less evident. Most of the points on this ventricle gave concordant curves which do not resemble one type of branch block curves more than the other. A single point (point *1*), however, gave curves which resemble those at present ascribed to left branch block in all leads, but do not resemble so-called right branch block curves in any lead. It should be noted that the greater thickness of the left ventricular wall and the fanwise spread of its conduction system make it more difficult than in the case of the right ventricle to so place a stimulus on the epicardial surface that it will spread over the muscle of this chamber in a manner similar to the natural one.

It is now necessary to examine the foundation upon which the current interpretation of bundle-branch block curves in man rests.

The pioneer work in this field was that of Eppinger and Stoerk[7] who studied two patients whose electrocardiograms constantly showed broad diphasic ventricular complexes, the initial deflections of which were upward in Lead I and downward in Lead III. The downward deflections in Lead III were thought to be comparable to the similar deflections which Eppinger and Rothberger obtained from an anus-oesophagus lead in a dog, the right branch of whose His-bundle had been damaged. They therefore diagnosed the condition in these patients as right branch block and at autopsy found lesions involving this branch of the bundle.

This work was confirmed by Lewis[13] in his exhaustive analysis of the electrocardiogram. He first showed that when in a dog either bundle branch was cut the excitation process reached the contralateral ventricle and spread over it in a normal manner, but that it did not reach the homolateral ventricle until later, and that it spread over this ventricle aberrantly. He concluded that the first portion of the initial phases of the abnormal ventricular complexes in right branch block was the graph of the normal spread of activity in the left ventricle, and that the corresponding portion of the left branch-block complexes was the graph of the normal spread of activity in the right ventricle. The former he called the levocardiogram and the latter the dextrocardiogram. In proof of this idea he showed that when the levocardiogram and dextrocardiogram were isochronously summated, the bicardiogram thus produced very closely resembled the normal electrocardiogram.

*This view was advanced some years ago by Fahr[6], as a result of theoretical considerations.

By determining the amplitude of the curves in each of the three leads at many isochronous points he demonstrated that the electrical axis of the heart rotated in a clockwise direction when the left bundle branch had been damaged and in an anticlockwise direction when the right bundle branch was rendered non-conducting. The rotation of the electrical axis shown by the ordinary concordant curves of the dog was much less uniform than that shown by the relatively rare discordant right branch block curves obtained from this animal and by the discordant curves of a large Rhesus monkey. Then with the work of Eppinger and Stoerk in mind he examined human curves of the type which they from their pathological studies believed to be characteristic of right bundle-branch block. He found that these also showed a rotation of the electrical axis in a counter-clockwise direction. He also analyzed a clinical curve of the opposite type, believed to represent left branch block, and found that in this case the electrical axis rotated in a clockwise direction. He pointed out that in dogs the behavior of the electrical axis during the inscription of the dextrocardiogram, or levocardiogram as the case might be, was in harmony with the spread of the excitation wave over the corresponding ventricle. At each instant the electrical axis assumed the direction of the average spread of excitation referred to the plane of the three leads, in so far as this could be determined from his previous studies of ventricular activation.

He concluded that the human levocardiogram was characterized by a diphasic ventricular complex the initial phase of which was upward in Lead I and downward in Lead III and that in the human dextrocardiogram the initial phase was directed downward in Lead I and upward in Lead III. This conclusion rests mainly upon the resemblance between the human curves now ascribed to right branch block, the relatively rare discordant right branch block curves of the dog, and the discordant branch block curves of the single Rhesus monkey examined. Since the electrical axis is derived from the ordinates of the deflection in the three leads a similarity in its direction, or changes in direction from instant to instant, is not more fundamental so it seems to us, than a similarity in the form of the electrocardiogram. Admitting that the resemblance referred to between certain clinical and certain experimental electrocardiograms supports the current interpretation of human branch block curves, it may be pointed out that even within a single species there is considerable variation in the form of the ventricular complexes obtained by cutting the branches of the His-bundle. This is shown by the right branch block curves of the dog which are sometimes discordant, although usually of the concordant type. It is also apparent that not all species of monkeys yield curves of the same kind; in contrast to the discordant curves obtained by Lewis from a *Rhesus* monkey. Wilson and Herrmann[20]

obtained concordant curves from a monkey of the genus *Cercopithecus*. If such differences exist between closely related animals even greater differences between animals and man are not improbable. The heart of man is much larger than that of the experimental animals, and this factor as well as differences in its position and in the distribution of its conduction system may influence the form of the human curves.

Aside from the experimental work of Lewis the studies of Eppinger and Stoerk are the chief evidence upon which the identification of the human levocardiogram rests and the identification of the human dextrocardiogram is largely inferential. Convincing as this classic paper is, there is one point where error might have been introduced. That is, the criteria for believing that the muscle strand which was interrupted by the discovered lesion was the right branch of the His-bundle were not given. This would perhaps seem unnecessary, but as the Purkinje tissue is differentiated only with difficulty from the surrounding muscle in man such evidence is of paramount importance for it is the keystone of the entire structure of the argument. While certain cases have been described in confirmation of the observations of Eppinger and Stoerk,[10] there have been about as many which contradict them[16, 19] and in most instances no lesions of any sort have been found[2] to account for the abnormal curves. Because of the unsatisfactory nature of these pathological studies any definite and well-controlled physiological observations bearing on this subject would seem to be preferable evidence.

The present authors believe that they have presented such physiological evidence in ascertaining the forms of the ventricular premature beats produced by stimulating accurately located points on the surface of the human ventricles. This evidence, as we have pointed out, indicates that the human levocardiogram is a broad notched diphasic curve the principal deflection of which is downward in Lead I and upward in Lead III, and that the human dextrocardiogram is a similar curve in which the main deflection is upward in Lead I and downward in Lead III.

3. *Ventricular Preponderance.*—It has long been known that disorders which tend to produce preponderant hypertrophy of the right ventricle, such as mitral stenosis and certain forms of congenital heart disease, are very frequently associated with electrocardiograms in which the chief initial deflection is downward in Lead I and upward in Lead III; and that disorders which tend to produce preponderant hypertrophy of the left ventricle, such as hypertension and aortic disease, are still more frequently associated with electrocardiograms of the opposite type. In conformity with the current interpretation of bundle-branch block curves it is at present held that the form of the electrocardiograms in question is dependent upon the relatively increased mass of the muscle of the right or left ventricle as the case may be. If what are now regarded

as right ventricular effects in the human electrocardiogram are in reality left ventricular effects and *vice versa,* some other explanation of the form of these curves must be offered which will account for the predominance of the effects of the smaller ventricle. It is possible that this may be brought about by changes in the position of the heart; that is to say, by rotation of the heart about is long axis produced by enlargement of the one or the other ventricle. It seems more probable, however, that it is the result of a defect in the conduction system of the enlarged ventricle which delays the activation of this chamber and permits the smaller ventricle to control the early phases of the ventricular complex. The conduction defect may be the result of mere lengthening of the conducting tracts of the enlarged ventricle, as Fahr[6] has suggested, or more probably of injury of these tissues resulting directly or indirectly from a prolonged increase in intraventricular tension.

Although this explanation of the curves under discussion is not entirely satisfactory, it is perhaps not less so than the one at present accepted. It accounts, for instance, for the serious discrepancies between the form of the electrocardiogram and the relative weights of the two ventricles found in some of the cases studied by Herrmann and Wilson.[8] It also accounts for the observation that Q is largest in Lead I in left and largest in Lead III in right ventricular preponderance. This deflection is the graph of the activation of the first ventricular region to which the excitation wave normally spreads; it is difficult to see how the location or order of activation of this region can depend upon the relative weights of the two ventricles. If, on the other hand, preponderance curves are the result of conduction defects the variations in the form of Q are easily explained since the earliest region to pass into the excited state will lie in the right or left ventricle according to the bundle branch affected. It may be pointed out here that in the electrocardiogram of the new-born infant, Q is largest in Lead III as in other curves which display right ventricular preponderance, which suggests that the form of the infant's curve is not dependent upon the relatively greater weight of the right ventricle, but upon some peculiarity of the conducting system or of the position of the heart.

SUMMARY

1. A study of the arrival of the excitation process at a number of points on the surface of the human heart with reference to the beginning of R in Lead II was made. It was found that the order of excitation differs in some respects from that found by Lewis and Rothschild in the dog. The earliest points were on the anterior surface of the right ventricle near the atrio-ventricular border. Our results sug-

gest that the conducting tracts in the right ventricle of man may differ from those of the dog.

2. The curves produced by stimulation of various points on the surface of the human heart were recorded in the three standard leads taken simultaneously. These curves indicate that:

(a) Ventricular premature contractions of right ventricular origin are represented in the electrocardiogram by ventricular complexes in which the chief initial deflection is upward in Lead I. Ventricular premature contractions of left ventricular origin are represented in the electrocardiogram by ventricular complexes in which the chief initial deflection is downward in Lead I.

(b) The clinical electrocardiograms at present ascribed to block in the right branch of the His-bundle indicate block in the left branch, and *vice versa.*

(c) In so-called left ventricular preponderance the electrocardiogram is dominated by right ventricular effects and *vice versa.*

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THE CORONARY ARTERIES OF THE DOG*

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IN THE course of an investigation[1] on the effect of experimental coronary occlusion, it was necessary to study the normal distribution of the coronary arteries in the dog's heart. Our results are somewhat at variance with the generally accepted statement that the coronary arteries of the dog are analagous to those of man. Any comparison of the effects of coronary occlusion in the dog and man must rest on a similar anatomical structure, origin, course and distribution. The literature is reviewed by Spalteholz[2] and need not be given in this paper.

METHODS

In all, 63 hearts were injected. The injections were made by the technique of Gross.[3] Briefly, this consists of irrigation of the vascular bed with warm water or salt solution (45° C.) and injection of a suspension of barium sulphate in gelatin. After injection, the extraneous injection mass is removed by washing and that in the vessels is hardened by immersion in chilled 10 per cent formalin. Twenty-four hours later, x-ray photographs are taken of the intact and sectioned heart. Routinely, we have taken one radiograph of the intact heart and one of the heart sectioned in such manner that the outer walls of each ventricle are dissociated from the septum. In all photographic reproductions, which accompany this paper, the central portion is the septum, the left portion is the outer wall of the left ventricle and the right portion is the outer wall of the right ventricle. Stereoscopic radiographs were taken of a few hearts. Some hearts were dehydrated and cleared in oil of wintergreen by the technique of Gross.[3]

THE GENERAL DISTRIBUTION OF THE CORONARY ARTERIES

The coronary arteries of the dog may be divided into four main branches—the right, the left anterior descending, the left circumflex and the left septal arteries. The left coronary arises as one stem in all cases. Within a distance of from 2 to 4 mm. it divides into three branches, septal, circumflex, and descending.

The septal artery, which varies in diameter from 0.5 to 1 mm., passes directly into the muscular portion of the interventricular septum and divides into two branches, an anterior and posterior. (Fig. 1.) From these, there are numerous small twigs which supply the entire central portion of the septum and anastamose with the descending left and circumflex left arteries. A few branches of the posterior ramus ascend to the membranous portion of the septum and supply the main stem of the bundle of His. It is important to note, that the course of this septal

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artery does not appear in the subepicardial fat and hence any experimental interruption of the septal circulation in the dog is extremely difficult.

The anterior descending branch of the left coronary artery, 1.5 to 2.0 mm. in diameter, courses in the subpericardial fat along the anterior interventricular sulcus to the apex of the heart. Three groups of branches are derived from this vessel, those to the septum, those to the right ventricle, and those to the left ventricle.

The septal branches, 12 to 20 in number, arise at right angles from the under surface of the vessel and penetrate the interventricular septum for a distance of 10 to 20 mm., where they establish contact and slight anastamosis with the terminal twigs of the anterior ramus of the left septal artery. The branches to the right ventricle, 4 to 6 in number, arise at right angles from the right side of the vessel and are distributed to the 6 to 8 mm. of the right ventricle nearest the anterior sulcus. The largest of these branches is the first, which supplies approximately one-half of the conus arteriosus and anastomoses freely with the conus branch of the right coronary artery. The branches of the descending left artery to the left ventricle, 3 to 5 in number, arise from the left side of the vessel at a 30° angle and are distributed to the anterior one-third of the outer wall of the left ventricle (Fig. 1).

The circumflex branch of the left coronary artery is the largest, varying from 2 to 3 mm. in diameter. It courses in the auriculo-ventricular groove from its origin to the posterior interventricular sulcus, where it turns toward the apex and forms the posterior descending artery. Four groups of vessels arise from the left circumflex artery; branches to the left ventricle, to the right ventricle, to the septum, and to the auricles. In the auriculo-ventricular sulcus, there arise 6 to 8 right-angle branches which are distributed to the posterior two-thirds of the outer wall of the left ventricle. (Fig. 2.) The first of these is constant and fills the angle between the circumflex and anterior descending left arteries. In 75 per cent of hearts it arises from the circumflex and in 25 per cent from the anterior descending left. From the posterior descending artery, the branches to the septum and to the right ventricle arise in an analagous manner to those of the anterior descending artery. The posterior descending artery usually continues over the apex and supplies the extreme tip of the right ventricle (Figs. 2 and 3). The auricular branches are two in number, a proximal and distal. The proximal artery arises from the upper surface of the circumflex artery, 3 to 7 mm. from its origin and supplies the anterior half of the left auricle, left auricular appendage, and the anterior half of the interauricular septum. The distal artery arises near the posterior interventricular sulcus and supplies the posterior half of the left auricle and a small portion of the central part of the interauricular septum. There are abundant anastamoses between these vessels and the auricular

Fig. 2.

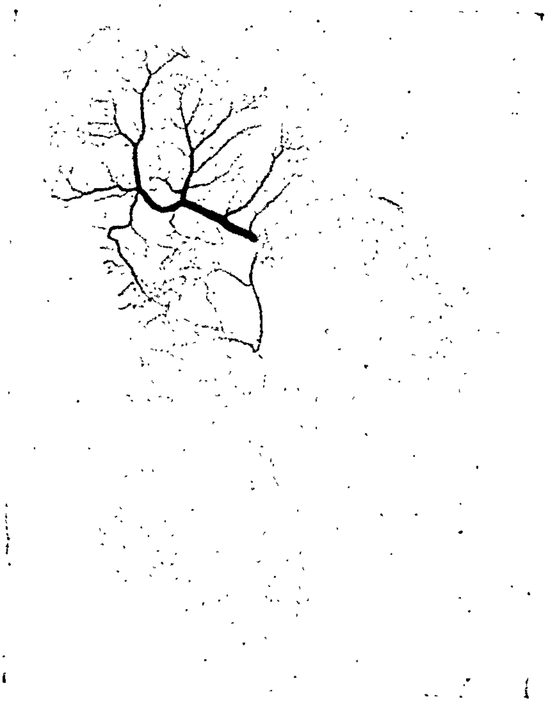

Fig. 4.

Fig. 1.

Fig. 3.

Fig. 1.—Injection of anterior descending left and septal left arteries. Note the [illegible] to the conus arteriosus, the definite central area of the septum supplied by [illegible] artery and the collateral filling of the circumflex left and right arteries.

Fig. 2.—Injection of circumflex left artery. Note the area at the extreme tip of the [illegible] ventricle supplied by this vessel and the collateral filling of all other vessels.

Fig. 3.—Injection of entire left coronary artery.

Fig. 4.—Injection of the right artery. Note the two auricular branches and the [illegible] anastomoses between them.

branches of the right coronary artery. It is important to note that in 63 hearts, the posterior descending artery was invariably a continuation of the left circumflex artery and never appeared as a continuation of the right artery. Gross[3] states that such a condition is observed in only

Fig. 5.—The region of the auricular arteries posterior to the aorta to show the abundant anastamoses between the right and left proximal auricular arteries.

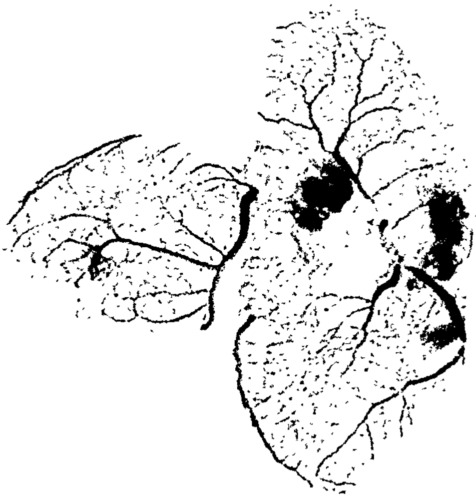

Fig. 6.

Fig. 7.

Fig. 6.—Experimental ligation of the anterior descending artery to show the filling of the vessel below the ligature through collateral channels. Compare with Fig. 7.

Fig. 7.—Experimental ligation of the anterior descending artery to show complete absence of collateral circulation. Compare with Fig. 6.

20 per cent of human hearts. The entire circulation of the left coronary artery is shown in Fig. 3.

The right coronary artery arises in 80 per cent of cases as a single vessel and in 20 per cent as two vessels. It courses in the auriculoventricular sulcus and gives auricular and ventricular branches (Fig.

4). The ventricular branches are 4 to 8 in number and pass perpendicularly down the surface of the right ventricle. The first branch is constant and is distributed to the conus arteriosus where it anastamoses freely with the conus branches of the anterior descending left artery. In 20 per cent of cases, it arises from the aorta independent of the main artery. The auricular branches are 2 in number, a proximal and distal. The proximal arises 2 to 8 mm. from the aorta and courses through the right auricle and auricular appendage where it anastamoses with the proximal left auricular artery posterior to the aorta. The distal auricular artery arises near the posterior interventricular sulcus and courses toward the mouth of the superior vena cava. In the region of the sino-auricular node it anastamoses with the right proximal auricular and both left auricular arteries (Fig. 5).

THE BLOOD SUPPLY TO THE SEPARATE PARTS OF THE HEART

In order to render the results more definite, the distribution of the vessels will be rearranged on the basis of the outer wall of the right ventricle, the outer wall of the left ventricle, the septum and the auricles.

The outer wall of the right ventricle is supplied by branches of the left anterior descending, the left posterior descending and the right coronary arteries. The left anterior descending artery supplies the 6 to 8 mm. of the outer right ventricular wall adjacent to the anterior interventricular sulcus (Fig. 1). In the region of the conus this supply is definite and extends over one-half of the entire conus. The posterior left descending artery supplies the extreme apex of the outer right ventricular wall (Fig. 2) and occasionally the 2 to 4 mm. of outer wall adjacent to the posterior interventricular sulcus (Fig. 4). The remainder of the outer wall is supplied by 4 to 8 perpendicular branches of the right artery, the first of which is constant and supplies one-half the outer wall of the conus. Anastamoses are abundant between the conus branch of the right and left anterior descending arteries, the perpendicular branches of the right and the left posterior descending arteries at the apex, and the perpendicular branches of the right artery and the right ventricular branches of the left anterior and posterior descending arteries.

The outer wall of the left ventricle is supplied by the left anterior descending and left circumflex arteries. The former is distributed to the anterior third and the latter to the posterior two-thirds. The angle between the origin of these two vessels is supplied by a branch, which usually arises from the circumflex (75 per cent), but occasionally from the left anterior descending artery (Fig. 3). The degree of anastamosis between these two vessels is variable, but is usually abundant. In Figs. 6 and 7 are two hearts, in which the left anterior descending artery was ligated during life. One hour after ligation the animal was killed and the heart injected. In one (Fig. 6) the anterior descending artery

filled from collateral anastamoses while in the other (Fig. 7) there was no collateral filling. Both were injected at 50 mm. of Hg pressure with all conditions the same. In only three hearts, have we observed complete absence of anastamoses to the left descending artery as shown in Fig. 7. It is possible that injections of the coronary arteries of the beating heart by the method of Wearn[4] would alter this conception of anastamoses. That the filling is not leakage by the ligature is evident from observation of the heart during injection, since the ligated vessel fills from below.

The muscular portion of the interventricular septum derives its blood supply from three sources, the left septal, the left anterior descending and the left posterior descending arteries, all branches of the left coronary artery. The left septal artery supplies the central portion while the septal branches of the two descending arteries send small twigs into the septum for a distance of 6 to 20 mm. The membranous portion of the interventricular septum is supplied in large part by branches of the right and left proximal auricular arteries and in small part by branches of the posterior ramus of the left septal artery. There are abundant anastamoses between these three sources of blood to the septum.

The delineation of definite areas of blood supply in the auricles is impossible because of abundant anastamoses (Fig. 6). The most extensive anastamosis occurs posterior to the aorta between the proximal right and left auricular arteries. The type of anastamosis corresponds to the third variation described by Kugel[5] in the human heart. In no instance have we been able to delineate a definite arteria anastomotica auricularis magna in the dog's heart. In numerous hearts, injection mass in the left coronary artery has been observed to flow across these vessels and fill the main branches of the right coronary artery. (Figs. 1, 2, 3.) No data on the ages of these animals are available and the relation of age to the amount of anastamoses is not known. We have not observed any differences in the hearts from manifestly young animals. In general the auricular branches of the right coronary artery supply the right auricle and those of the left coronary the left auricle.

The sinus node derives its chief supply from the right distal auricular artery but in this region there are abundant anastamoses with the other three auricular arteries. This is in agreement with the findings of Meek, Keenan and Theisen.[6] The auriculo-ventricular node is supplied by the right and left proximal auricular arteries and the bundle of His by the left septal artery.

SUMMARY

1. The coronary arteries of the dog differ from those of man in two major points: the presence of a distinct and separate septal artery as

a branch of the left coronary artery; and the formation of the posterior descending artery by the left in all cases rather than in 20 per cent as in man.

2. The origin and course of the septal artery renders experimental ligation of it difficult. It is improbable that previous investigators have interrupted the blood supply to the septum.

3. Anastamoses between the coronary arteries and their branches are extremely abundant in the dog's heart.

I wish to thank Dr. L. Katz for the specimens used in this investigation and Dr. H. T. Karsner for aid in the preparation of the manuscript and photographs.

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VARIATIONS IN HEART-BLOCK SOMETIMES ATTRIBUTED TO A SUPERNORMAL RECOVERY PHASE*

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IN CASES of heart-block a certain peculiar variation has occasionally been observed; auricular beats occurring soon after systole excite the ventricle, while others occurring a little earlier or later in the cycle elicit no ventricular response. Explanations of the variation have logically referred it to those processes which the authors regard as responsible for the block itself. In accordance with the prevailing notion regarding heart-block they attribute this unusual variation to a transient change in A-V "conductivity," even though they are not in agreement regarding the exact causes of such change in conduction. Other authorities, however, have reminded us that the general problem of heart-block is one of too great complexity to permit in every case an interpretation that is concerned only with conduction.

Our case is published because such variations of heart-block are rare, because it shows certain points of difference from the others, and because in it a different explanation of the variation in block (and of the block itself) appears to be indicated.

CASE REPORT

The patient was a woman fifty-four years of age who entered the Barnes Hospital August 15, 1927, complaining of dyspnea, orthopnea and slow pulse. Dyspnea had begun seven months before admission. Two months later she had consulted a doctor because of an upper respiratory infection. At that time strychnine, iodide and digitalis were ordered. Exact amounts could not be determined, but it was thought that the amount of digitalis was quite small, and the record states that she had had "very little digitalis." There had been giddiness on a few occasions, and in June she experienced a syncopal attack. For the following week she was in bed, and during that period there were several recurrences of syncope. Since that time she had been in bed for the most part and had had no further symptoms.

At examination the patient was in good general condition. There was slight cyanosis of the lips, and the face was somewhat pale. The heart was slow and the impulse vigorous. The rhythm consisted of single and paired beats with a total rate of 45 per minute. There were periods during which only single beats occurred, the rate at such times being 25 per minute. At other times (and this rhythm predominated) the beating was persistently bigeminal. There was a soft murmur accompanying the first sound of the single beats. This systolic murmur was noted also with the first of the bigeminal beats, but not with the second. The blood pressure was 180/50 mm. The Wassermann test was negative. Tests of kidney function gave normal results. The patient remained in the hospital five days, her stay being without important incident. At frequent examinations the heart rate was invariably slow and the rhythm essentially the same as on admission.

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THE ELECTROCARDIOGRAMS

Electrocardiograms were made on August 15, 17, and 20. On August 17, atropine sulphate, gr. 1/40, was administered intravenously, and records were taken at frequent intervals following the administration. Each record shows a high degree of A-V block, and in each the ventricular rhythm is modified in the manner referred to above. Before discussing the details of this unusual modification of rhythm and its probable import, it will be in order to describe briefly the electrocardiograms that portray it.

The record taken on admission (Fig. 1) shows an auricular rate of 81. There is a high degree of A-V block, only each third auricular impulse producing a ventricular contraction. The conduction time of such auricular impulses as excite the ventricle is not lengthened (P-R, 0.16 sec.). The regular 3:1 sequence, however, is frequently interrupted in the following manner: that auricular beat which occurs immediately after a ventricular systole excites the ventricle again, giving for two successive cycles 1:1 rhythm. Immediately after such bigemini the auricle again fails to excite the ventricle, and 3:1 block supervenes. This interruption of ventricular rhythm, while frequent, is by no means invariable.

The record of August 17 (which is not reproduced) made just before administration of atropine, shows an auricular rate of 100, and for the most part an uninterrupted 3:1 A-V sequence. The P-waves that fall first after ventricular systole are each exactly superimposed on the T-wave, and no bigemini such as are exhibited in Fig. 1 occur. Toward the end of this (long) record, however, the rate of the auricle becomes a little slower and ventricular escape takes place. Under this independent ventricular rhythm, the P- and T-waves are no longer superimposed, and between their peaks appears a space the width of which increases with successive ventricular beats, the T-wave falling earlier and earlier with reference to the P-wave. At a place in the record where this space between T and P becomes comparable to that shown in Fig. 1, the P-wave is followed by a ventricular complex.

It will be noted, then, that this unusual ventricular response occurs, upon occasion, following both types of ventricular systoles; after those consequent upon ventricular escape as well as after those due to effective auricular stimuli in partial heart-block. But in both instances the ventricle responds only to certain ones of the postventricular auricular beats. To which of these auricular stimuli does the ventricle respond, and to which is it silent? What are the conditions limiting ventricular response to particular auricular beats? It was found that those auricular impulses which reach the ventricle during a fixed time interval in its cycle excite it to contraction. This sharply defined interval, measured from the beginning of the R-wave, falls near the end of the T-wave. Other auricular stimuli which begin a little earlier

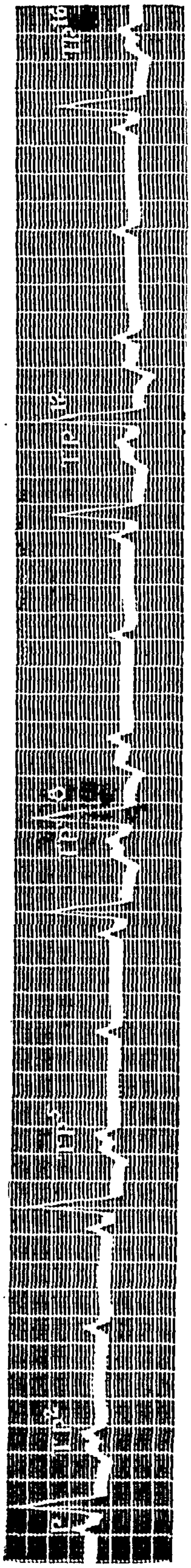

Fig. 1.—Electrocardiogram (Lead II) made August 15, 1927. Discussion in the text.

or a little later elicit no response. *Either they fail to reach the ventricle, or reaching it, they are ineffective.* In order to elicit a response, therefore, an auricular stimulus falling after a ventricular systole, must have its beginning during a certain period following the systole.

Whether or not any of the P-waves in a given record were located within this area of response was found to depend on several factors. (*a*) Consideration had first to be given to the type of *ventricular mechanism.* When complete A-V dissociation (ventricular escape) obtained, P-waves fell at quite different intervals after the beginning of R, and sooner or later an R-P interval occurred whose length was such as to place the P-wave within the area of response. Auricular rate, therefore, was not a factor. (*b*) With 3:1 block, on the other hand, *auricular rate* became a determining factor. For, since the P-R interval remained constant, the auricular rate determined the time interval at which P fell after R, i.e., the R-P interval. (*c*) *Duration of systole* was found to be a factor of crucial importance in both types of ventricular mechanism. It was stated that an auricular impulse, in order to be effective in producing a bigeminal beat, must arise at such a time as would allow it to reach the ventricle in that phase of its cycle corresponding in the electrocardiogram to a certain *critical zone* near the end of the T-wave. Now the duration of systole, as indicated by the duration of the ventricular complex, was longer for idioventricular beats than for beats of supraventricular origin. Since, then, the position of this critical zone, which may be designated "C," or the R-C interval, differed in the two types of systoles, it follows that effective auricular beats occurring after one type of systoles, must of necessity begin (measured from R) at a time interval different from that of the beats which follow the other type. The proposition may be stated in another way: An auricular beat so placed as to excite the ventricle after one type of ventricular systoles, must fall at a different time interval in order to be effective with the other type. It follows that the R-P intervals of effective auricular beats must differ in the two types of mechanism.

Another factor has a well-known influence on the duration of systole, i.e., ventricular rate. Particular reference will presently be made to the influence of ventricular rate upon certain other important features of rhythm displayed by the electrocardiograms. So far as its effect upon the occurrence of bigeminal beats is concerned, it may be said that the rate with 3:1 block differed very little from that following ventricular escape, and that only slight variations in ventricular rate occurred in either type of mechanism. Differences in ventricular rate in a given record had little to do, therefore, with variations in ventricular response. But the basic rate of the ventricle at a given time was an important factor in determining whether or not definitely placed auricular beats could elicit a response.

The net result of the above factors may be quite simply stated: Whether or not a given auricular beat occurring soon after ventricular systole is found to excite the ventricle, depends upon the relation of the R-P interval to the R-C interval. Now, it has just been shown that the R-C interval depends upon the R-T interval. It follows, therefore, that ventricular response is determined by the relationship of R-P to R-T. But since with 3:1 block, R-P is determined by the auricular rate, and since R-T depends upon the rate of the ventricle, it follows further, that the matter of ventricular response is determined (1) in 3:1 block by the relationship between auricular rate and ventricular rate; (2) with ventricular escape, by the chance position of the P-wave in the ventricular cycle. It may be stated further that, in the case of 3:1 block, variations in the R-P:R-T ratio in a given record, are due almost entirely to *variations in auricular rate,* differences in the R-T intervals, as above noted, being of slight extent because of the relatively slight changes in ventricular rate.*

The above statements receive abundant confirmation in the records. Fig. 2 is a record in Lead III made during a forced respiration. It shows an arrhythmia of the auricles to which attention has frequently been called in reports of heart-block. That interauricular interval which includes ventricular systole is shortened. But these intervals themselves show a variation that is a part of a general change in auricular rate with respiration. At the right end of the record the rate is essentially the same at the beginning. Between these portions it becomes slower and then faster. With the slowing, the R-P interval increases and thus the P-wave is placed too late for its impulse to reach the ventricle during C. With acceleration the R-P interval shortens until P falls early enough to reach the ventricle before the termination of C. These observations are verified not only by measurements of corresponding auricular cycles but also by mere inspection of the successive T-P intervals.

Similar tests applied to Fig. 3 demonstrate the same facts. The sixth interauricular interval is longer than the third. Auricular rate was becoming slower, and that the retardation was continued is shown by the fact that the seventh interval is somewhat longer than the fourth. This is indicated also by the longer T-P interval in the seventh cycle. Auricular rate then became faster, and the tenth P-P interval was short enough for the P-wave to fall within the critical zone C. Fig. 3 illustrates also the later position of C with escaped beats. Although the P-wave, following the escaped beat near the right end of the illustration, falls at a time later after the (projected) beginning of

*It should be borne in mind that this statement regarding ventricular rate refers only to the question so far discussed, i.e., the production of bigemini. Only the interval between a preceding ventricular beat and the *first* beat of the bigemini can be used in considering the question. The R-R interval between the beats of the bigemini themselves represents a much faster rate and is important in another matter which will presently receive consideration.

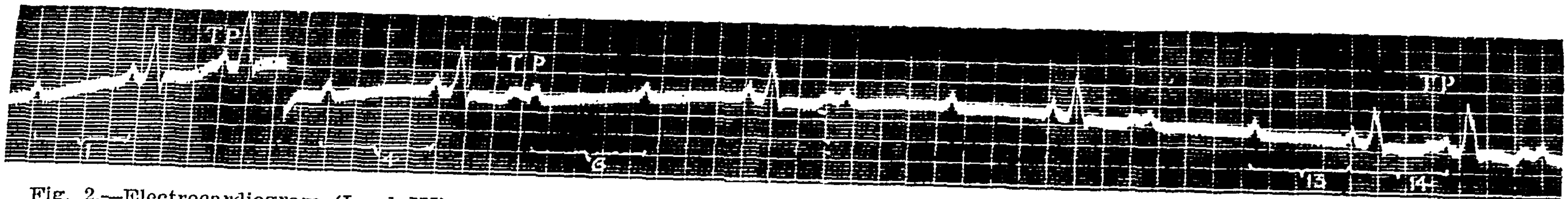

Fig. 2.—Electrocardiogram (Lead III) made August 15, 1927. The brackets 1, 4, 6, etc., indicate corresponding P-P intervals. The auricular rate becomes slower in the midpart of the illustration, and then becomes faster again (respiratory). Note the short T-P intervals with the faster rate at the beginning and at the end of the illustration where the bigemini occur.

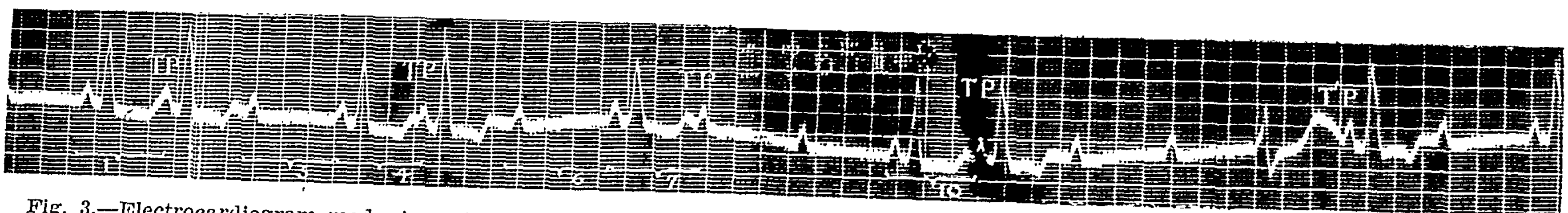

Fig. 3.—Electrocardiogram made August 17, 1927 (six and one-half minutes after the administration of *atropine*, *Lead II*). Average auricular rate 85. Note the different lengths of the T-P intervals and the failure of the ventricular response with the long interval above bracket 7. Near the right end of the illustration ventricular escape occurs. With this "escaped" beat the R-P interval requisite for ventricular response is different from that of the other type of systoles.

R than does the P-wave closing the seventh interauricular interval, it is, nevertheless, early enough to excite the ventricle, while the other falls too late to do so. In the light of Figs. 2 and 3, the interpretation of Fig. 1 becomes obvious. With an auricular rate of 82, the postventricular P-waves are falling at such times after R that the impulses reach the ventricle near the termination of C. Impulses from P_8 and P_{12} fall just within, those from P_2, P_5, and P_{16} just without its confines.

Just as a slow auricular rate (long R-P interval) may cause the auricular beat to fall too late to excite the ventricle, so with a faster rate of the auricle its impulse may occur too early (short R-P interval). Such a situation is shown in Fig. 4. The auricular rate in this illustration averages about 95 as compared to an average rate of 85 in Fig. 3. The rates at the extremes of Fig. 4 are identical. There is slight acceleration in the first third of the record, however, the maximum rate being attained about the sixth and seventh interauricular intervals, after which point the rate becomes slower. (Compare interval 5 with 1, 8 and 15; also interval 6 with 2, 9 and 16.) With the acceleration the P-wave closing the sixth interval falls too early and does not excite the ventricle, the rate at that moment being about 100.

Brief consideration should be given to the mechanism responsible for limiting ventricular response to only one auricular stimulus. In the records so far exhibited the P-wave following the second beat of the pair does not again excite the ventricle and thus continue 1:1 rhythm, because of the following facts: (1) The auricular rate, having shown temporary acceleration in the manner that has been described in heart-block and to which reference was made above, becomes slower again. This alone might on occasion be sufficient to terminate the 1:1 rhythm. (2) Another factor, however, operates toward the same result. With the occurrence of the bigeminal beat, the rate of the ventricle is abruptly accelerated to about three times its original level, and the R-T interval of the second beat, therefore, is materially shortened. As a consequence of these changes in ratio of R-P to R-T, the impulse from the P-wave which follows the bigemini falls beyond the critical zone.

A. Duration of the Critical Zone.—Consideration has just been given to the interplay of factors responsible for placing the P-wave so that the impulse falls within or without the critical zone C, and to those factors which change the location of this zone itself. Whether or not the stimulus of a given P-wave falls within the confines of this zone, obviously must depend upon the duration, or the width, of the zone. If the width were of sufficient extent, all the P-waves in question would be effective, only 1:1 response would obtain, and there would be no block. It is, in fact, because of its very limitations that cases such as ours come under observation to present a special problem in heart-block.

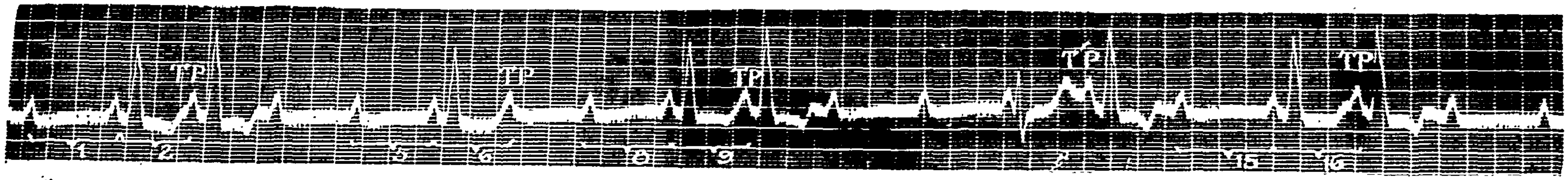

Fig. 4.—Eleven minutes after atropine (Lead II). Average auricular rate 95. Bigeminal beating occurs consistently except after the P-wave which closes the sixth P-P interval. Auricular rate is fastest at that point, and the P-wave falls too early to be effective.

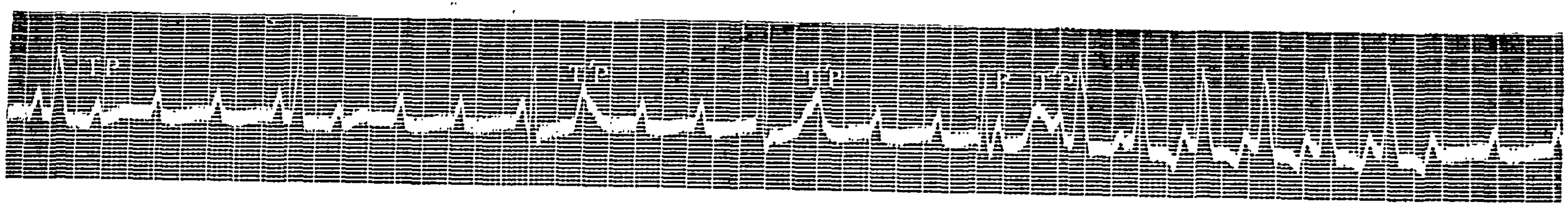

Fig. 5.—Seventeen and one-half minutes after atropine (Lead II). Auricular rate 132. Note that the continued 1:1 rhythm at the right of the illustration is initiated with the second P-wave following an escaped beat. Discussion in the text.

Exact determination of the confines of this zone, with either type of ventricular beats, is difficult, but its approximate location can be fixed. In the case of those beats of supraventricular origin it is arrived at as follows: In Fig. 1, where the P-waves were placed so that their stimuli were reaching the ventricle near the end of C, the longest interval between the beats of the bigemini is 0.7 of a second. P-waves placed even a little later, elicited no ventricular response. Under the conditions of that record, therefore, C ended at about 0.7 of a second after the beginning of R. In Fig. 3 the longest interval (that between the third pair) is about 0.64 of a second after the beginning of R. The ventricular rate in the latter case is somewhat faster than in the former, and this, as above noted, placed C a little earlier. In Fig. 4, on the other hand, the stimuli from auricular beats are falling near the beginning of C. The shortest R-R interval of bigeminal beats (that of the second pair) is 0.59 of a second. An auricular stimulus which arises earlier, reaches the ventricle before the onset of C. Under the conditions recorded in Fig. 4, therefore, the beginning of C is about 0.59 of a second after the beginning of R. It may be stated, then, that with a ventricular rate of 33 per minute (Fig. 4), C begins about 0.59 of a second after the onset of R. With a rate of 30 per minute (Fig. 3), it ends about 0.64 of a second after R, and with a rate of 27 (Fig. 1), it ends about 0.70 of a second after R. From these determinations it would appear that its endpoint is doubtless still earlier with a rate of 33 than with the slower rates, and since its end point with a rate of 30 is 0.64 of a second after R, it probably ends earlier than that with a rate of 33. Now its beginning with the latter rate is 0.59 of a second after R. Its duration, therefore, at a rate of 33 per minute is probably less than 0.05 of a second.

Knowledge of the duration of C may be important from two viewpoints. First, it may be of value in trying to determine the nature of the process responsible for this removal of block over such a brief time interval. Second, it fixes the condition under which 1:1 rhythm may be continued over more than two cycles.

B. Continued One-to-One Response; Conditions Requisite for Its Inception and Continuation.—Fig. 5 is a portion of the record made seventeen and one-half minutes after the administration of atropine. The auricular rate is 132. The record contains both types of ventricular complexes, and the zone C, therefore, is located at different intervals in the ventricular cycle. The first ventricular complex is of supraventricular form, and the P-wave that follows it occurs too early for its impulse to reach C.* 'Ventricular escape takes place, the postventricular P-wave falling later and later with reference to R. But with these "escaped" beats C occupies a later time interval, and even

*With the same ventricular rate in Fig. 4, it was seen that C begins at about 0.59 of a second after the beginning of R.

though the P-waves fall later than did the one first recorded, they are still too early for the auricular stimuli to reach C. Following the fifth ventricular complex, however, the second auricular beat falls at the proper time and a ventricular systole results. But with the occurrence of this systole ventricular rate has become much faster, and the next auricular impulse, though falling at an interval after R which is essentially the same as that recorded at the beginning of the figure, is not now too early to reach C, because the latter, with the faster ventricular rate, has moved forward in the cycle. It is now early enough to catch the auricular impulse, and another ventricular response, therefore, takes place. With this beat *the short R-T interval is continued.* Now the rate of the auricle also is faster than that recorded in any of the previous records, and this produces a short R-P interval; the resulting R-P to R-T ratio being such as to maintain the 1:1 response. The duration of C, its "width," however, is limited, and the auricular stimuli are doubtless falling near the edge of a narrow zone. After a few beats an auricular impulse, because of slight disturbance of the R-P to R-T ratio, falls outside its confines and fails to excite the ventricle.

This figure 5 is a part of a long record showing the same succession of events many times repeated. One-to-one rhythm was invariably initiated in the same manner. It appears, indeed, that it is only in this way, i.e., following an escaped beat with a (second) P-wave falling well on the down slope of T, and at the same time a fast auricular rate, that it is possible for sustained 1:1 rhythm to be initiated. For with an auricular rate fast enough to maintain it in the presence of the (resulting) rapid ventricular rate, it cannot be initiated following a systole that originates in 3:1 block. The ventricular rate in such a case, as noted above, is relatively very slow, and the zone C of such a systole, therefore, is too late for the auricular impulse of such a rapidly beating auricle (and consequent short R-P interval) to reach it. One-to-one rhythm having been initiated, however, in the manner described, the length of R-T is then brought into the proper ratio to R-P, and 1:1 response continues.

It will be observed, then, that both of the unusual modifications of ventricular rhythm recorded in this case, bigeminal beating and continued 1:1 response, are referable to the relationship of the R-P interval to the R-T interval. The effect of atropine in removing the block appears to result only from the acceleration of auricular rate produced by it, and to depend in nowise upon any effect on A-V conduction.

COMMENT

The removal of block in this case occurs under two circumstances: (1) at the end of a long period, in a manner common to partial heart-

block and calling for no special comment, (2) over a brief span of ventricular systole, before the termination of the above-mentioned period. It is this unusual feature which has sometimes been regarded as resulting from an overswing in the recovery of the A-V tissues and for which, in the present case, a different explanation appears to be indicated.

Two aspects of the problem must be considered: (1) the site at which the removal of block is effected, and (2) the nature of the process effective for so brief an interval at that site. All authors who have reported such cases regard the A-V tissues as the site in question, only Lewis and Master[1] considering the possibility of any other location. There is not such agreement, however, with regard to the second aspect of the problem. Lewis and Master regard the cause as a "supernormal" recovery phase. Ashman and Herrmann,[2] although mentioning possible causes of improvement in conductivity other than an overswing in the recovery curve, favor the same explanation. Wolferth[3] agrees that such a supernormal phase might explain the phenomenon, but he offers alternative explanations to account for the temporary improvement in A-V conductivity.

Whatever the cause of the block recorded in our case, wherever its site, it appears that there is little ground for assuming that its transient removal results from an overswing in the recovery curve of A-V conductivity in the sense that the term was employed by Adrian and Keith Lucas.[4] They found that frog's nerve when bathed in fluid that was relatively acid, showed, during its recovery after excitation, an overswing in the curve of recovery, a "supernormal" phase. They found the same overswing, under like conditions, in the recovery curve of frog's heart muscle after contraction. The records of our case indicate clearly that the relief of block resulted from some effect of the preceding ventricular systole. Its constant position in the ventricular cycle, its different time relationship with systoles of different lengths, admit of no other interpretation. But the records do not imply that the site of this effect is in the A-V tissues. Systole might conceivably produce an overswing of conductivity in the A-V tissues either directly or indirectly. A retrograde impulse sent into the bundle by a ventricular contraction might directly effect such a result. The A-V tissues in their recovery from the conduction of such an impulse might exhibit a supernormal phase. Ashman and Herrmann, indeed, employed this conception in their Case 1 in which the relief of block occurred after an idiopathic ventricular systole from which presumably an impulse might have been sent in retrograde fashion into the bundle. But our case exhibited the phenomenon during partial (3:1) block. The impulse entered the bundle from above, and not as a result of ventricular contraction. Since the systole was of supraventricular origin, therefore, any effect upon the A-V tissues induced by it must have been

an indirect effect. Whether some such indirect effect of ventricular contraction might change the A-V tissues so as to produce exactly the conditions necessary for an overswing in the recovery curve, an overswing, furthermore, which must exactly coincide with the time of the oncoming auricular stimulus, at present would appear to be problematical. No explanation of such a process is proposed by Lewis and Master. It is possible, of course, that systole might temporarily heighten A-V conductivity in some way other than by producing a "supernormal" recovery, a solution of the problem favored by Wolferth.

Neither the precise effect of ventricular contraction that is responsible for the removal of block for so brief an instant, nor the exact site of its application, can be determined merely by a study of clinical records, nor can the cause of the antecedent block. It appears unnecessary to employ various assumptions referring it to the A-V tissues. The simplest explanation would refer it to the ventricle itself, provided such an explanation be in accordance with accepted notions about heart-block.

The theory of heart-block proposed many years ago by Erlanger[5] takes into account not only different degrees of A-V conductivity but also different levels of ventricular irritability (or excitability) and different strengths of auricular stimuli as well. It presupposes that certain auricular impulses may pass the A-V conducting system and still find the ventricle unresponsive. This conception, indeed, is entertained by authorities who, at the same time, are inclined to refer all instances of heart-block to "defective conductivity" alone. They, in common with others, explain the failure of an auricular impulse which, if conducted normally, would reach the ventricle during its refractory phase (following a spontaneous ventricular systole), not as depending upon a temporary defect in the A-V tissues, but as due to a temporary change in ventricular excitability. The block in the present case, indeed, may as well be the result of lowered excitability of the ventricle as of lowered conductivity of the A-V tissues. With this in mind we are prepared to accept the obvious implication of the records which appear to refer variations in the block to variations in ventricular excitability. By the application of Erlanger's theory the phenomena recorded in our case are explained as follows: Due to a lesion in the A-V tissues, which reduces the strength of auricular impulses, or to a condition of lowered excitability in the ventricular muscle, the auricular stimuli arriving at the ventricle are below threshold. After a long recovery period ventricular excitability rises to such a level that the next auricular stimulus is effective (3:1 block). The resulting systole, in some way, causes the curve of ventricular excitability to rise sharply for a brief instant, after which it falls and resumes its gradual rise. If an auricular stimulus happens to arrive

at the ventricle at the moment when excitability is high, another contraction is effected. This second systole produces another brief rise in ventricular excitability which may or may not coincide with the arrival of an auricular impulse—depending on the ratio of R-P to R-T, as already discussed.

As to the process responsible for this transient rise in ventricular excitability, we offer no surmise. An overswing in the recovery curve of ventricular excitability (a possibility suggested by Lewis and Master), if indeed such a phenomenon occurs in mammalian heart muscle, would occupy a phase in the ventricular cycle corresponding essentially to that of the critical zone C during which auricular stimuli are effective. Its location, when observed, is near the end of the refractory period. Its position in the ventricular cycle, therefore, while constant for systoles of the same length, would show with systoles of different lengths correspondingly different intervals after the beginning of R—a characteristic feature of our records and one which it would be difficult to correlate with A-V conductivity.

It is possible that some circulatory or other effect of systole, at present unknown, may occupy only such a phase in the ventricular cycle. Just how systole produces in certain cases of heart-block the auricular arrhythmia referred to is a conspicuous example of some such influence at present not understood. If the cause of the block was indeed a depression of ventricular excitability, then it may be that systole effected an improvement in the physiological properties of the ventricular muscle which, for a brief period, raised ventricular excitability. Until more is known of the effects of systole on various cardiac properties a solution of the problem cannot be reached.

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THE ADRENALIN TEST IN HYPERTENSION*

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INTRODUCTION

IN 1894, Oliver and Schafer,[1] and independently of them, Szymonovicz and Cybulski[2] demonstrated that adrenalin had a marked pressor effect on the cardiovascular system. In 1909 Eppinger and Hess[3] used adrenalin as a pharmaco-dynamic test for the symptom complexes which they called sympathicotonia and vagotonia. It was not until three years later, however, that Bauer[4] wrote his fundamental paper on the adrenalin test, and by giving adrenalin subcutaneously, established the character of the reaction of normal individuals. He emphasized the dissociation of the adrenalin effects and the peripheral vasodilatation, and concluded that though patients may have varying vegetative tonus, the use of the drug as a method of differentiating between sympathicotonia and vagotonia was not justified.

The adrenalin test has been used in many clinical conditions and occasionally as a method of differential diagnosis. Goetsch[5] employed it to aid in the recognition of hyperthyroidism but was criticized by Sandiford,[6] Peabody[7] and others. In the clinical states of vascular hypertension the results have been variable. Kylin[8] was the first to call attention to the inconspicuous response met with in cases of hypertension when 1 c.c. of adrenalin is injected subcutaneously. In this finding he varied from Clough[9] who had found exactly the opposite response. Brems[10] and many other authors agreed with Kylin; to these, references may be found in his papers.

Sanguinetti[11] and, independently of him, Csepai[12] believed that by administering adrenalin subcutaneously the factor of difference of absorption is added. They suggested intravenous administration of a much smaller dose. The blood pressure response of the patient with hypertension to this changed technic soon gave rise to another argument. One group, led by Hetenyi and Sümegi[13] and Csepai[12, 14] found universally in hypertension an increase in the adrenalin response, while Deicke and Hülse[15] and others asserted that this increased response was only present when renal damage had occurred.

At present there is no unanimity of opinion concerning the question. This study, therefore, was undertaken for the purpose of determining whether the hypertensive response differs in any characteristic manner from the normal response, and if it does, whether this reaction throws any light upon hypertension. At first an attempt was made to deter-

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mine whether the blood pressure response to adrenalin would be consistent when the test was repeated in the same individual. It was soon found that there were variations so striking as to warrant special study. These have been investigated both in patients with hypertension and in normal individuals.

PROCEDURE AND MATERIAL

Forty-three persons were selected for adrenalin tests. These were performed before breakfast with the patient still in bed. Some ambulatory patients in whom these conditions were not obtainable rested for twenty to thirty minutes before the test. The cuff was always placed on the right upper arm and the same mercury manometer was used throughout the experiments on the same person. The systole was determined as the highest level where all the beats were plainly audible, and the diastole was the level where the clear sound changed to a muffle. If no such transition was marked, the diastole was taken as the lowest level where the sounds were distinctly heard. The difficulty of this determination did introduce a personal factor into the diastolic readings. Readings were taken every three minutes until a sufficient number were obtained to form some opinion as to the level and variability of the blood pressure. Then 1 c.c. of saline solution was usually injected subcutaneously into the left deltoid region, and readings were continued while the reaction produced by the prick of the needle was observed, usually for nine or ten minutes. Then 1 c.c. of clear colorless adrenalin was injected into the left deltoid region and the site of the injection was thoroughly massaged for thirty seconds. Occasionally the dose was one-half c.c. Thereafter frequent blood pressure and pulse readings were taken, until the reactions immediately following the injection had subsided. Usually blood pressure and pulse readings were taken every three minutes for ninety minutes after the injection of adrenalin. During the early part of the work the pulse was not counted. Occasionally the observation lasted more or less than ninety minutes. Omitting the saline injection the test was then repeated one to four times. All tests were done by me, personally, but most routine blood pressures were taken by the clinical staff. The subcutaneous method was used because it seemed the simplest and because the effects were so protracted that they could be studied in detail. In my opinion absorption did not vary sufficiently to influence the test.

The patients were arranged in the following groups: (1) normal controls, that is, persons with normal cardiovascular systems; (2) patients with pronounced hypertension; (3) patients with early or intermittent hypertension; (4) finally a small group with miscellaneous conditions in which we thought our findings might throw some light upon the manifestations in the patients with hypertension. Included in this group were cases of nephritis, hyperthyroidism, and enlargement of the heart without hypertension. Some of the subjects in groups 1 and 3 were members of the University Hospital Staff.

RESULTS

A. *The Normal Response to Adrenalin.*—When adrenalin was injected into thirteen normal persons, there followed a higher systolic blood pressure, a lower diastolic pressure, and a more rapid pulse rate. The increase in systolic pressure varied from 15 to 58 mm. Hg, the maximal pressure being reached in from 11 to 46 minutes. The immediate response varied from 8 mm. in 22 minutes to 38 mm. in three and a half minutes. In three cases the pressure increased suddenly.

The decrease in the diastolic pressure amounted to from 8 to 38 mm. Hg and occurred in 5 to 39 minutes and as a rule the pressure returned to normal in 60 to 90 minutes. The pressure usually fell rapidly and returned slowly to normal, but some irregularities occurred, possibly because of errors in reading.

TABLE I

THE INCREASE OF SYSTOLIC BLOOD PRESSURE AFTER 1 C.C. OF ADRENALIN IN TWELVE NORMAL INDIVIDUALS

PATIENT NO.	TIME OF OBSERVATION (IN MINUTES AFTER INJECTION OF ADRENALIN)	EXTENT OF INCREASE	
		FIRST TEST	REPEATED TESTS
18	7	20	2
19	4	6	12
20	8½	14	54
21	4	0	26
22	3½	38	60
23	1	0	44
24	4	4	36
25	7	12	20
26	4	–4	16
27	3	30	66
28	7	30	36
29	1	2	36

TABLE II

THE DECREASE OF DIASTOLIC BLOOD PRESSURE AFTER 1 C.C. OF ADRENALIN IN TWELVE NORMAL INDIVIDUALS, THE TIME WHEN THIS DECREASE OCCURRED AND THE TIME CONSUMED ON THE RETURN OF THE PRESSURE TO NORMAL

CASE NO.	MAXIMUM DECREASE (MM. HG)	TIME OF MAXIMUM DECREASE (MINUTES)	TIME OF RETURN
18	38	23	86
19	10	5	45
20	26	7	67
21	20	14	56
22	?	?	—
23	20	39	96
24	8	6	9
25	14	10	71
26	24	37	106
27	26	27	78
28	20	30	60
29	18	17	72

The increase in heart rate came in some cases before the systolic rise, in other cases later. It bore no relation to the blood pressure changes. In the few cases which were examined for this point, the increase lasted longer than the changes of either the systolic or the diastolic pressures.

When the tests were repeated in the same individual, the systolic changes remained of the same general character, but in eleven of the twelve cases where the test was repeated in 48 hours or later, the response changed qualitatively, becoming more sudden and more intense.

The findings in Case 18 may be due to delayed absorption, for when the blood pressure finally increased it rose more sharply than on the first occasion. In cases 25, 27, and 30, a second injection was given in three hours or less. The rise was slower, less extensive and poorly sustained. The nature of this change in response was not clear. Possibly it was due to fatigue of the mechanism which determined the response.

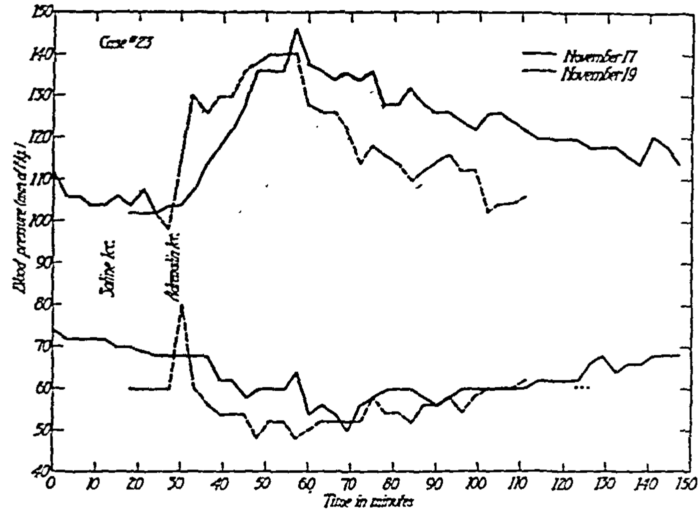

Fig. 1.—Showing the gradual increase and still more gradual decrease of systolic blood pressure after adrenalin in a normal person. On repeating the test, the pressure increased suddenly.

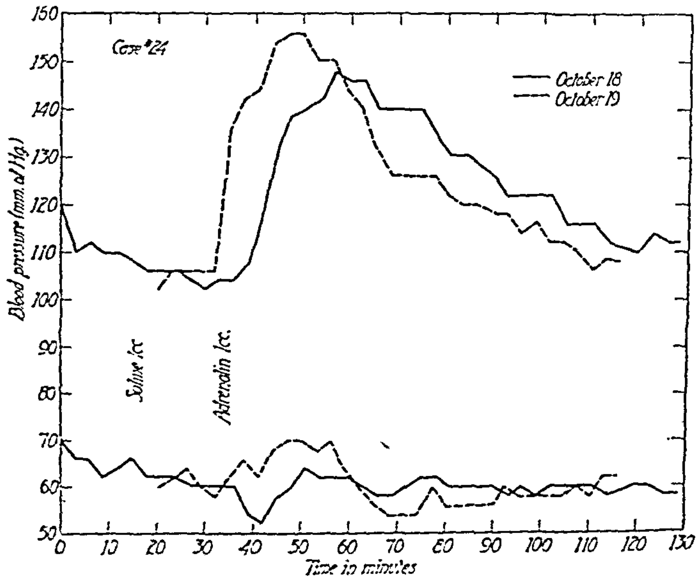

Fig. 2.—Showing a more sudden increase in a normal person. Also accentuation on repetition.

Although in the repeated tests the form of the diastolic blood pressure curve was fairly well retained, it might be modified by large or sudden increases of systolic pressures. Such systolic changes, how-

ever, did not necessarily affect the diastolic pressure. The increase in heart rate was not changed in the repeated tests.

B. *The Adrenalin Response in Pronounced Hypertension.*—Nine cases of this group showed a decrease of systolic blood pressure after adrenalin. This might or might not be preceded by a rise. On account of the spontaneous variations in the blood pressure of patients with hypertension it is not possible to describe any of these changes as adrenalin effects. Six cases showed a sharp systolic rise (Table III). In three of these six the increase was followed by a fall below the original level.

TABLE III

THE MAXIMAL INCREASES OF SYSTOLIC BLOOD PRESSURE (IN MM. HG AFTER A FIRST AND AFTER A REPEATED INJECTION OF 1 C.C. OF ADRENALIN INTO HYPERTENSIVE PATIENTS, AND THE TIME (IN MINUTES) CONSUMED OBTAINING THESE INCREASES*

CASE NO.	FIRST INCR.	TEST TIME	REPEATED INCR.	TEST TIME	CASE NO.	FIRST INCR.	TEST TIME	REPEATED INCR.	TEST TIME
1	8	1	60	3	11	58	10	66	4
2	10	3	72	3	12	74	4	48	4
3	12	7	76	2½	13	100	3		
4	20	13	94	4	14	88	3	64	2½
5	22	1	72	4½	15	30	3	42	4
6	6	7	44	3					
7	6	4	66	4					
8	16	2½	54	2½					
9	44	4	74	2					
10	18	4	66	2½					

*In the cases of the first column, the increase, which after a first injection is slight, is accentuated and the time is somewhat shortened after the repeated tests. In the second column the increase after the first injection is considerable. After the repeated injection it is not accentuated, but the time is somewhat shortened.

TABLE IV

MAXIMAL INCREASES OF SYSTOLIC BLOOD PRESSURE (MM. HG) AFTER A FIRST AND AFTER A REPEATED INJECTION OF 1 C.C. OF ADRENALIN INTO SIX CASES OF EARLY OR INTERMITTENT HYPERTENSION, AND THE TIME CONSUMED (IN MINUTES) TO OBTAIN THIS INCREASE

CASE NO.	FIRST INCREASE	TEST TIME	REPEATED INCREASE	TEST TIME
31	0	0	30	7
32	20	4	42	3
33	16	22	20	2
34	18	19	18	5
35	18	5	20	2½
36	20	19	36	2½

On fourteen patients with hypertension the tests were repeated at intervals varying from 12 hours to 30 days. In all of them the repeated test showed a sudden and intense increase of the systolic pressure. In the nine cases where the response to the first test had been indeterminate the contrast between the first and the repeated tests was most striking (Fig. 3). In one case the response to the first injection was so violent that the test was not repeated. In three cases

where the first reaction had been brisk, the response on repetition was greatly intensified (Fig. 4). In two cases the repeated response was slightly less but otherwise similar to the first one. When the test was repeated after 48 hours in case 14, the reaction was considerably diminished and case 6 failed to respond 24 hours after the first test. Both, however, gave an active response respectively 8 and 2 days after the first injection. The findings are summarized in Table IV and the protocol of a typical case is appended below.

A decrease of the diastolic pressure of from 8 to 34 mm. Hg occurred in 13 to 54 minutes. When the systolic pressure rose sharply the

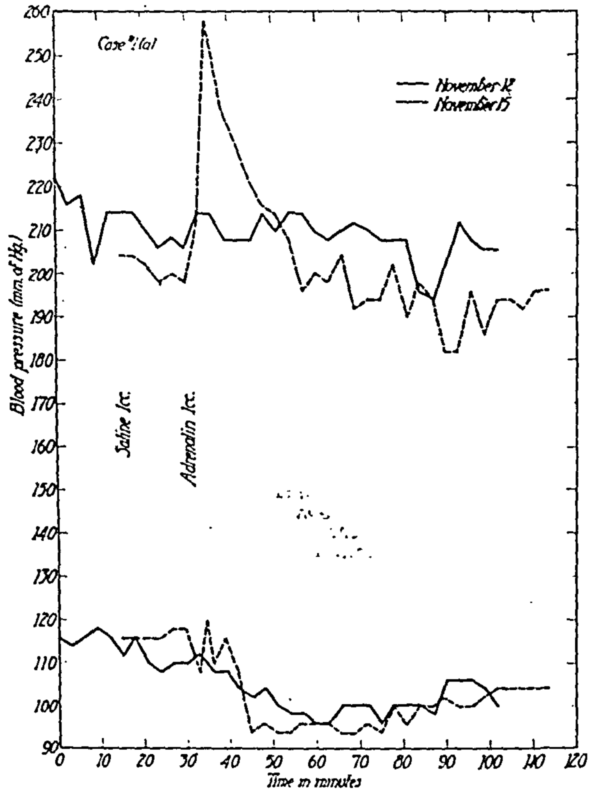

Fig. 3.—Showing lack of response to 1 c.c. of adrenalin when first administered to a hypertensive patient. On the repeated test three days later the injection was followed by an intense reaction with subsequent decrease to sub-initial level. Decrease of diastolic pressure.

diastolic fall was preceded by an increase corresponding to the systolic rise. The diastolic pressure changes were not as great as the systolic. The return to normal was so slow that in only two cases of the series did it occur during the period of observation. With repeated tests the diastolic response was but slightly modified except in the cases where the systolic pressure rose sharply. Then the diastolic, as in the first tests, showed a corresponding, moderate, transient increase. There was no evidence that the changes in the diastolic pressure are related in any way to those of the systolic pressure. Also in the repeated tests the diastolic pressure was slow in returning to normal. There was no

change in the diastolic reaction after repeated injections of adrenalin. The acceleration of the heart rate varied from case to case without relation to the changes in the blood pressure. When the tests were repeated no important change in response was observed, except during very severe systolic reactions. Then the pulse rate increased considerably for a few minutes. This was thought to be due to cardiac distress rather than to a direct adrenalin effect.

Thus the response in the patients with hypertension to first injections of adrenalin fell into two groups. In one no certain effect could be

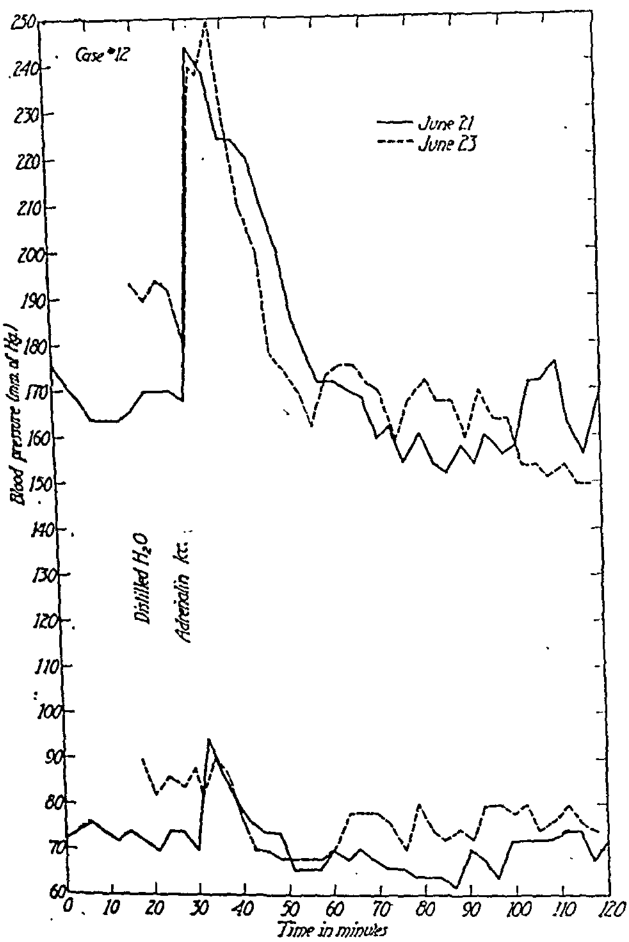

Fig. 4.—Showing immediate intense reaction of hypertensive patient to adrenalin. On repeating the test two days later, a similar response was obtained.

ascribed to adrenalin and in the other the response was intense. The reactions of the diastolic blood pressure and of the heart rate were marked by no division into groups.

The protocol of patient No. 2 is given in some detail as an example of the general reactions observed during the procedure.

CASE REPORT

Mr. J. T., aged 47 years, was known to have had hypertension for one month. The hospital diagnosis was primary hypertension with some renal insufficiency. He was given adrenalin 1 c.c. (Fig. 3). This caused no definite change in his systolic blood pressure. Three days later the test was repeated. The systolic pressure now

rose 60 mm. Hg, in three minutes, and he felt very sick. He became pale and was very tremulous; for 20 minutes he had a severe headache. The elevated blood pressure immediately began to fall and in 20 minutes had reached the original level. Later it decreased an additional 20 mm. Also this time the diastolic pressure decreased, except for a slight increase while the systemic pressure was highest. As the systolic pressure decreased, the patient felt better, but all through the day he suffered from paroxysmal tremulousness. When the test was repeated the next day, a similar reaction followed.

Eighteen days after the initial injection no immediate systolic reaction took place; an increase of 30 mm. Hg half an hour later could not be considered an adrenalin effect as it fell within the spontaneous variations in hypertension. The following day there was no systolic change after adrenalin. The diastolic change was constant; a gradual decrease lasted through the period of observation.

C. The Adrenalin Response in Cases of Early or Intermittent Hypertension.—In the group designated by pronounced hypertension systolic pressures of 186 or over and diastolic pressures over 100 mm. Hg were

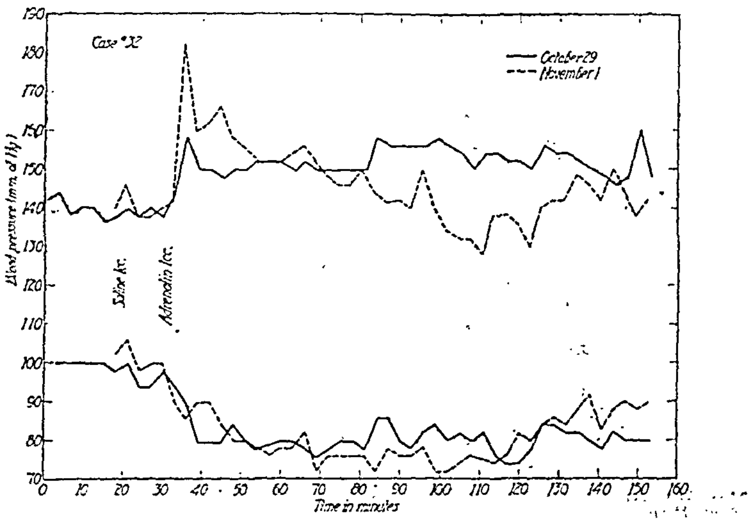

Fig. 5.—Showing slight response to adrenalin in a case of early hypertension. On repeating the test a sudden and intense response was obtained, though of smaller magnitude than in advanced hypertension.

found. The group designated by early or intermittent hypertension had diastolic pressures below 100, and highly variable systolic pressures, at times more than 150 and at others less than 130. The marked spontaneous variations of the systolic pressures frequently obscured the results of the injections. The injection of adrenalin was always followed by an increase in systolic pressure, but this exceeded 20 mm. in one instance only. Although in three cases the pressure subsequently sank below the initial level, this decrease was within the normal limits of spontaneous variations. The increase in pressure was much less than was usual in normal persons. When the tests were repeated 2 to 4 days later this group showed a marked change in response, which was now sharp and immediate although less than in advanced hypertension. (Fig. 5, Table IV.) The diastolic pressure changes in the individuals with hypertension differed from those in normal persons mainly in

that they returned more slowly to normal. In this respect the cases of intermittent hypertension distributed themselves evenly; three did and three did not present normal diastolic pressures at the end of the test.

DISCUSSION

A. *The Normal Variation in Adrenalin Response.*—Our results, which show that the systolic blood pressure increased from 15 to 38 mm. after the subcutaneous injection of adrenalin, agree well with those of Bauer,[4] Brems,[16] and others. I have found in the literature of well documented researches no investigation on the constancy of the test when repeated in the same person. Almost everyone who injected adrenalin repeatedly

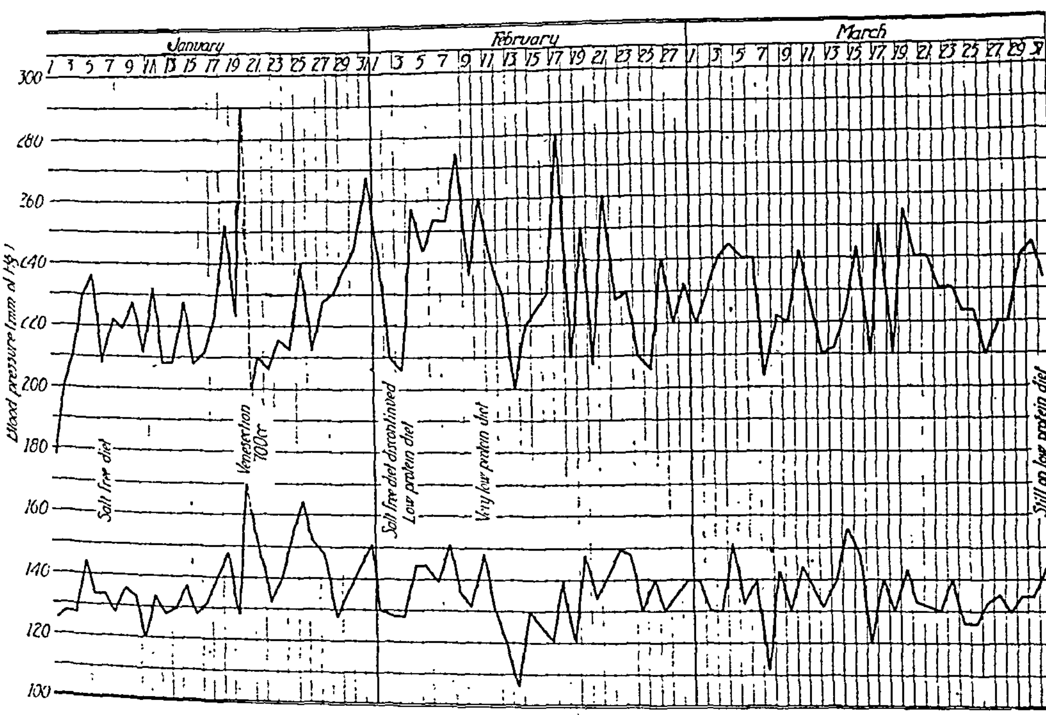

Fig. 6.—Showing diurnal variations of blood pressure in a case of severe hypertension of ten years' standing. The systolic pressure shows much greater variations than does the diastolic.

introduced some factor between the two injections and ascribed any change to this factor. Brems[17] worked with calcium and the adrenalin test; Billigheimer[18] with protein diet; Mahler[19] with glycosides; Peabody[7] with infections.

I had observed the decrease of the diastolic pressure on patients before I learned of it from the literature. Independently Dr. Ulrich suggested that this effect was due to a peripheral vasodilatation. Later we found that Bauer,[4] Hotz,[20] Brems[17] and others had observed a lowered diastolic pressure and had already suggested a similar interpretation.

The normal response to adrenalin is characterized by a more or less rapid, but rarely sudden, increase of systolic blood pressure, followed by a somewhat slower return to normal level, and by a decrease in

minutes. When the test is repeated the increase in blood pressure is more sudden and intense, but the general configuration of the blood pressure curve is not affected.

B. *The Response of the Hypertensive Patient to Adrenalin.*—It is now well known that even in advanced hypertension the blood pressure may vary considerably. Figure 6 illustrates the daily variations of blood pressure in a patient who had had hypertension for ten years.

It seemed worth while to make a mathematical observation to ascertain whether this difference in variability of blood pressure between normal persons and hypertensive patients was mathematically a true difference or whether it was only apparent. This was done under the direction of Dr. Scammon in the Department of Anatomy.

For this purpose 36 blood-pressure readings were obtained from two patients with hypertension and two controls (Table V). The readings were taken about 12 at a session, at two-minute intervals, the various series being taken on different days, but under identical conditions so as to include both the minute-to-minute and day-to-day variations.

The average of the readings was calculated for each person as well as the probable error of the average, and the standard deviation was then calculated in the usual manner and its probable error determined.

Each control was now compared with the two persons with hypertension and the difference between the standard deviations was calculated as was also the probable error of this difference.

The standard deviation is an expression of the variability of the blood pressure, and in order to show a real difference, the difference between the standard deviations

$$\frac{S\ D_h - S\ D_n}{\text{Error}\ (S\ D_h - S\ D_n)} = \text{should be above three,}$$

where $S\ D_h$ = standard deviation of the pressure in hypertension, and $S\ D_n$ = standard deviation of the normal pressure. It will be seen from Table V that in all four cases this ratio exceeded three; the variability of blood pressure in patients with hypertension mathematically exceeded that of the controls. This tendency to spontaneous changes and the excessive reactions to stimuli had to be taken into consideration when evaluating the response to adrenalin. It is not surprising, therefore, that the patient with hypertension reacted with excursions of his blood pressure far in excess of those seen in normal persons, in some cases only after a preliminary administration of the drug. This might be followed by an abrupt fall to a sub-initial level.

With a few exceptions the curves obtained from patients with hypertension were easily distinguished from the normal curves. One patient with hypertension (No. 3) had after the first injection a slowly but definitely increasing blood pressure, while in one of the normal in-

TABLE V

SHOWING A TRUE MATHEMATICAL DIFFERENCE BETWEEN THE VARIABILITY OF SYSTOLIC BLOOD PRESSURE IN NORMAL AND HYPERTENSIVE PERSONS*

NAMES	NORMAL		HYPERTENSIVE		DIFFERENCE BETWEEN STANDARD DEVIATIONS	PROBABLE ERROR OF DIFFERENCE BETWEEN ST. DEV.	RATIO OF DIFFERENCE AND OF PROBABLE ERROR OF DIFFERENCE BETWEEN ST. DEV.
	AVERAGE AND PROBABLE ERROR OF AVERAGE	STANDARD DEVIATION AND PROBABLE ERROR OF ST. DEV.	AVERAGE AND PROBABLE ERROR OF AVERAGE	STANDARD DEVIATION AND PROBABLE ERROR OF ST. DEV.			
Normal A—Hypertension X	114.9 ±1.29	3.40 ±0.27	167.5 ±1.88	13.60 ±1.07	10.20	1.10	9.28
Normal A—Hypertension Y	114.9 ±1.29	3.40 ±0.27	193.1 ±2.16	7.61 ±0.60	4.21	0.66	6.38
Normal B—Hypertension X	109.3 ±1.22	4.27 ±0.34	167.5 ±1.88	13.60 ±1.07	9.33	1.12	8.33
Normal B—Hypertension Y	109.3 ±1.22	4.27 ±0.34	193.1 ±2.16	7.61 ±0.60	3.34	0.69	4.84

*All figures on the basis of 36 readings.

dividuals (No. 28) the wave rose to a high maximum within a few minutes of the injection of adrenalin. During the repeated tests several of the normal controls gave an intense response. But in these cases the subsequent decrease was slower than in hypertension and the blood pressure did not reach the sub-initial levels seen in the patients with hypertension. While no single feature of the reaction was of absolute value in determining the difference between the normal response and that in hypertension, the reaction in the two groups was on the whole strikingly different.

In the cases of hypertension the response of the diastolic pressure was not grossly different from that of normal individuals. Generally, however, there was a greater lag in its return to the initial level.

A striking feature in the analysis of the tests on patients with hypertension was the division into two groups: in one (which we shall call Group A) the response of the systolic blood pressure was insignificant and formed a marked contrast to the intense response obtained when the test was repeated about forty-eight hours later. In the other group (which is designated as group B) the response was marked both to the first and to subsequent injections. There were no clinical features by which the two groups could be distinguished from one another. It was particularly noted that the response was not determined by the amount of kidney damage.

In analyzing the material the groups were easily separated, though some of the patients who gave an insignificant response did show a small sudden rise of blood pressure immediately after the injection. The possibility that this was spontaneous or due to psychic causes could not be excluded.

In early or intermittent hypertension the conditions were intermediary between the two previous groups. The response to a first injection was approximately as in the persons with hypertension of group A, and less than in the normal person. On repetition the response was markedly accentuated but less than in the patients with hypertension of Group A. In the repeated tests the average increase of blood pressure after adrenalin was 83 per cent over the increase after the first injection; in marked hypertension of Group A it was increased 412 per cent, and in normal persons it was 21 per cent.

The maximum reading was reached sooner in advanced than in early hypertension and sooner in early hypertension than in normal persons. After the repeated injection the maximum reading was reached as soon in early hypertension as in advanced hypertension.

Also the variations in blood pressure after the first and the repeated tests were analyzed for the purpose of determining to what extent the change in response was mathematically true. For this purpose the average blood pressure was computed from about thirty readings after the giving of adrenalin and the probable error thereof was determined.

The standard deviation from this average, that is, the variability of the pressure after adrenalin, was calculated with its probable error. This was done both in the first and the repeated tests, and the two standard deviations were compared. If the standard deviations (that is, variability of blood pressure, in this case increase of blood pressure) should be significantly greater in the repeated than in the first test, the difference between the standard deviation of the first and the repeated tests should exceed three times the probable error of this difference.

This difference was significant in the cases of hypertension of Group A where there was a marked contrast between the first and repeated tests and in one case of intermittent hypertension, but not in the controls nor in the persons with hypertension of Group B who reacted well to the first injection; nor in the most cases of early or intermittent hypertension.

The Mechanism of the Adrenalin Response in Hypertension.—In the discussion by other authors of the adrenalin reaction in hypertension various interpretations were given of the results obtained. Investigating these results two questions presented themselves: Is the reaction, as obtained in hypertension, specific for that condition; and is there in hypertension any one demonstrable factor upon which the reaction depends?

I believe that the response characteristic of hypertension is the sudden intense increase of systolic blood pressure, and that this response is in some hypertensive individuals obscured by the lack of reaction to the first injection. This will be discussed below. I found it also in some normal persons, though the excursions were not quite of the magnitude observed in individuals with hypertension. Goetsch[5] and others obtained a similar response in hyperthyroidism. This I could confirm. Peabody[7] found it in certain cases of functional cardiovascular disease. This sudden intense response is by some considered characteristic of sympathicotonia, and without accepting or denying that doctrine one must admit that the response in hypertension may also be found in conditions other than hypertension.

The factors upon which the sudden increase in blood pressure depends in patients with hypertension have been considered. The reaction is not dependent upon the height of the blood pressure at the time of the test or on the general level of blood pressure of any individual.

Patients suffering from hypertension with equally high blood pressures, either did not respond or showed an intense increase of pressure to the first injection of adrenalin. The intense reaction might be absent when the blood pressure was elevated, but might occur in persons suffering from hypertension with pressures at many varying levels and might be found in patients with hyperthyroidism where the systolic pressure was normal. The response was intense not only as regards the

increase of pressure but also as to the suddenness with which this pressure was obtained.

One patient (No. 16) reacted to adrenalin like a case of hypertension, and the first injection was followed by no certain blood pressure changes. At the subsequent test an intense rise occurred. He had much clinical evidence of hypertension and a blood pressure which varied considerably from time to time and from beat to beat, but the systolic variations were between 108 and 135.

The response does not depend upon demonstrable cardiac or renal factors. It was found both with and without cardiac enlargement. Two cases of early nephritis reacted like normal persons. A case of advanced nephritis with a very high blood pressure gave a response as intense as any other hypertensive patient. Kylin[21] has stated that the blood calcium influences the blood pressure and the adrenalin reaction. In one patient where the parathyroid glands had been accidentally removed, and where the blood calcium could be regulated at will, I had an opportunity of examining the blood calcium both in relation to the height of the blood pressure and the adrenalin reaction. The three factors were not related. The adrenalin test was originally introduced as a diagnostic test for sympathicotonia and it might be asked if the intense reaction obtained in hypertension indicates that state. Adrenalin affects a number of functions, ordinarily under the control of the sympathetic nervous system: for instance, in the cardiovascular system, the blood pressure, the pulse rate, the conduction of impulses in the heart and the irritability of the cardiac muscle; but only the blood pressure response is increased in hypertension. If by sympathicotonia we are to understand the single manifestation of increase in blood pressure, then the response in hypertension could be considered sympathicotonic, but if sympathicotonia embodies a general hypersensitiveness to agents affecting the sympathetic nervous system, then this isolated sensitiveness of the systolic blood pressure cannot be so considered.

The view is prevalent in the literature that adrenalin given subcutaneously causes a peripheral vasoconstriction. I was unable to correlate this opinion with the findings of a decrease in diastolic pressure and on Dr. Ulrich's suggestion I was led to assume a peripheral vasodilatation. In a later study of the literature it was found that many authors have confirmed this view.

Kahn[22] noticed that in pulse tracings after adrenalin the pulse curve dropped more quickly than in controls, showing that the artery emptied faster. Bayliss[23] showed that when the intra-aortic pressure increased a generalized vasodilatation occurred. This reflex took place through increased aortic pressure and not through increased intracranial pressure.

Von Anrep[24] found by plethysmographic observations that the limb volume passively followed the pressure in the brachial artery, and Rosenow[25] believed the dilatation was a simple passive process caused by an increased load of blood thrown into the limb circulation, but Bayliss'[23] observation, that he obtained vasodilatation in the head and neck of a dog which was supplied from another heart-lung preparation, has shown that the vasodilatation was a reflex, and von Anrep[26] was unable to obtain any direct local reaction to changes of blood pressure by changing the pressure in a closed carotid artery.

Bauer in 1912[4] demonstrated that the low diastolic pressure meant peripheral vasodilatation, but his finding was frequently overlooked. Some authors when acquainted with Bauer's argument maintained their belief in vasoconstriction but transferred the site to the splanchnic area (Bauer,[4] Rosenow,[25] Pophal,[27] Hotz,[20] Horning,[28] Lyon,[29] Brems,[17] and others). This view was introduced into the German literature by Biedl[30] who in his *Innere Sekretion,* quoted from Oliver and Schäfer.[31] These authors had stated: "It may fairly be assumed that although we are unable to record any plethysmographic observations on the intestine, the great rise of blood pressure which invariably follows the injection of the extract is in all cases due very largely to the contraction of the arterioles of the splanchnic area." The experimental data underlying this assumption were not conclusive, and confirmatory evidence has not been observed in the later literature.

The systolic blood pressure is the outcome of two main factors: the velocity given to the blood stream by the contraction of the heart muscle and the resistance of the peripheral vascular system. The former acts during systole only, the latter during both systole and diastole. In the adrenalin test there is an increase of the pressure during systole only while there is no increase during diastole. Therefore, the increase of blood pressure must be due to the factor which acts during systole, the cardiac contraction. Dr. Ulrich originally suggested this mechanism and in a later study of the literature many authors were found to confirm this view. When auscultating the aortic area after giving adrenalin, the first sound was greatly accentuated but not the second, as would have been expected if the heart were working against increased peripheral resistance. I interpreted this increase of the first aortic sound as being due to augmented muscular vigor. Gottlieb[32] on the basis of adrenalin effect on the chloralized heart called attention to the importance of the cardiac factor in the reaction and in 1900 showed a tremendous augmentor effect of adrenalin on the isolated heart lung preparation.[33] Clough[9] also expressed the opinion that we are dealing primarily with a cardiac reaction rather than a peripheral one.

Lee Gunning[34] observed that in a dog, where the blood pressure varied in the different arteries, adrenalin produced the same absolute increase in all arteries irrespective of the initial pressure. A peripheral mechan-

ism might have been expected to produce a less regular response. Pilcher[35] caused a rise in the diastolic pressure by producing vasoconstriction of the peripheral circulation. Von Anrep[36] found that the secondary rise of blood pressure after splanchnic stimulation, which he attributed to liberation of adrenalin from the adrenals, bore a distinct relation to the tone of the heart. He also showed the heart's action to be the cause and not the result of the blood-pressure change; especially as hearts which worked against a peripheral resistance were not stimulated to greater efforts as were adrenalized hearts.

Thus confirmatory evidence is not lacking that in the clinical adrenalin response we are dealing essentially with a cardiac functional test.

All these patients with hypertension had blood pressures which were subject to great variations and I finally concluded that adrenalin response in hypertension is a manifestation of the general instability of the pressure in hypertensive individuals. This agrees with the finding that persons who had no hypertension, but who had given this kind of response, also had unstable vasomotor systems.

The Lack of Response to the First Injection in Some Hypertensives.—It is difficult to explain why an indeterminate response was obtained in some patients with hypertension when adrenalin was administered the first time. Clinically these cases differed in no way from those of the other group.

Some physiological experiments seem to resemble this reaction of hypertension. Sawitsch and Speranskaja-Stepanowa[37] found that cats with experimentally elevated pressures responded to adrenalin with irregular increases or even decreases of blood pressure. Gottlieb[33] investigated the cardiac reaction to adrenalin while the heart of the heart-lung preparation was working first against increased and thereafter against normal resistance. The reaction was much smaller when the resistance was higher. Cannon and Lyman[38] found that the initial peripheral tension determined the blood-pressure excursion after adrenalin; as the pressure increased, the excursion decreased and might even become negative. These findings were confirmed by Hartman.[39] Lyon[40] stated that "when the resting levels differ, the blood-pressure response to uniform doses of adrenalin varies, the magnitude of the disturbance diminishing as the resting level rises." In all these experiments the reaction to adrenalin was diminished when the heart worked against increased pressure, but clinically the same type of reaction was seen in case No. 16 where the blood pressure was within normal limits.

SUMMARY

1. It appears from the literature that the response to adrenalin in the patient with hypertension differs from that of the normal person, but the evidence as to the variations in response is contradictory.

2. Under approximately standard conditions series of subcutaneous injections of 1 c.c. of adrenalin were given to a number of normal persons, patients with hypertension, and others in whom the reaction was thought to throw light on the phenomena observed in hypertension.

3. Persons with normal cardiovascular systems responded with a slow rise and a subsequent slower decrease of pressure. While the height of the excursion was but slightly accentuated after subsequent injections, the time consumed in reaching the maximum height of the pressure was markedly shortened.

4. The cases of hypertension fell into two groups which were clinically indistinguishable. In the first group no definite change could be ascribed to the first injection of adrenalin, while the other cases of marked hypertension responded with a brisk and intense increase of systolic blood pressure. When the test was repeated all the patients with hypertension responded with intense rises of pressure. In cases of early or intermittent hypertension the findings were like those of the former group of advanced hypertension, but less pronounced.

5. Statistically it was found that the ratio of the difference and of the probable error of difference between the standard deviations from the average readings following the first and the repeated injections of adrenalin was significant in the first group, in those hypertensive patients in whom the response was absent on the first injection.

6. The diastolic pressure decreased after all the injections but the time required to return to normal was longer in the patient with hypertension than in the normal person. It was not influenced by repetition of the test.

The increase in heart rate and the occurrence of cardiac irregularities were not influenced by the state of hypertension or by repetition of the test.

7. The blood pressure reaction of adrenalin in hypertension did not depend on the level of the blood pressure, the size of the heart, presence or absence of kidney disease, or the level of the blood calcium. No satisfactory explanation could be offered for the absence of response in some individuals with hypertension or for the change in response between first and subsequent tests.

8. The clinical adrenalin reaction is not due to peripheral vasoconstriction. In fact a vasodilatation is present which indicates that the systolic rise is of cardiac origin. The intense increase in the patient with hypertension is thought to be related to the general instability of the hypertensive blood pressure. This instability is briefly discussed and considered mathematically.

This work was done under the direction of Dr. Henry Ulrich to whom I am gratefully indebted for many practical suggestions.

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ELASTICITY (EXTENSIBILITY) OF THE AORTA OF HUMAN BEINGS*

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A FAIR number of investigations have been made on the physical properties of the aorta of human beings. Most of these studies have been concerned with the elasticity of strips of the aorta, whereas some were directed toward the properties of internal pressure. By elasticity of vascular tissue is meant its power of yielding to a force and of resuming the original form when that force is removed. Herringham and Wills[1] determined that practically all aortas, when placed in physiological saline solution for five minutes, after they had been stretched with weights up to 200 gm., returned to their original form, and, therefore, that aortas are almost perfectly elastic. They also showed that the elasticity of the aorta depends chiefly on the amount of elastic and of connective tissue in the media and their reciprocal relations.

The following data of previous investigators have been accepted by us as being established: Post-mortem rigidity of the muscular media is negligible in the aorta of human beings.[3] Until putrefaction is far advanced the curve of elasticity of any aorta remains the same.[5] Only a very small amount of elasticity is lost over a long period of time (months) when the strip of aorta is kept constantly in physiologic saline solution, when the stretching is performed in that solution. The imperfection of elastic resiliency and the increase in extension are both dependent on the amount and the duration of the stretch.[7] Curves taken slowly (a half hour) are of the same form as those taken rapidly (two to three minutes[5]). Longitudinal strips taken from different sections of the aorta give the same curves and one strip is honestly representative.[2] The elasticity of longitudinal strips is less marked and less important than that of transverse strips.[2, 5]

That elasticity is dependent on age has been definitely determined, and it has been stated that elasticity (extensibility) increases from birth to the age of twenty years, after which there is a decline toward zero in senescence. Parallelism has not been established between the condition of the heart, general nutrition of the body or existing diseases and the elasticity of the aorta. Most authors agree that parallelism between loss of elasticity and degree of arteriosclerosis does not exist.

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OBJECT AND METHOD OF STUDY

We have devised a simple apparatus for measuring the extensibility of approximately identical, transverse strips of the aorta, and with it have determined this property as exemplified in 100 aortas of human beings. The object in view has been to correlate this property with age, sex, blood pressure, degree of visible arteriosclerosis, thickness of the wall of the vessel, and cause of death. The first portion of the opened aorta was removed from the unembalmed body and was placed in physiological saline solution, in which it remained for a variable length of time, usually a few hours. The piece of aorta was then placed, endocardium downward, on a flat board and the loose fascia adjacent to the adventitia was stripped off. A brass plate, 6 cm. long and 1 cm. wide, held with a handle, was placed on the vessel transversely, just above the attachment of the aortic valve, and pressure was applied evenly while with a sharp razor blade the section thus fixed by the plate

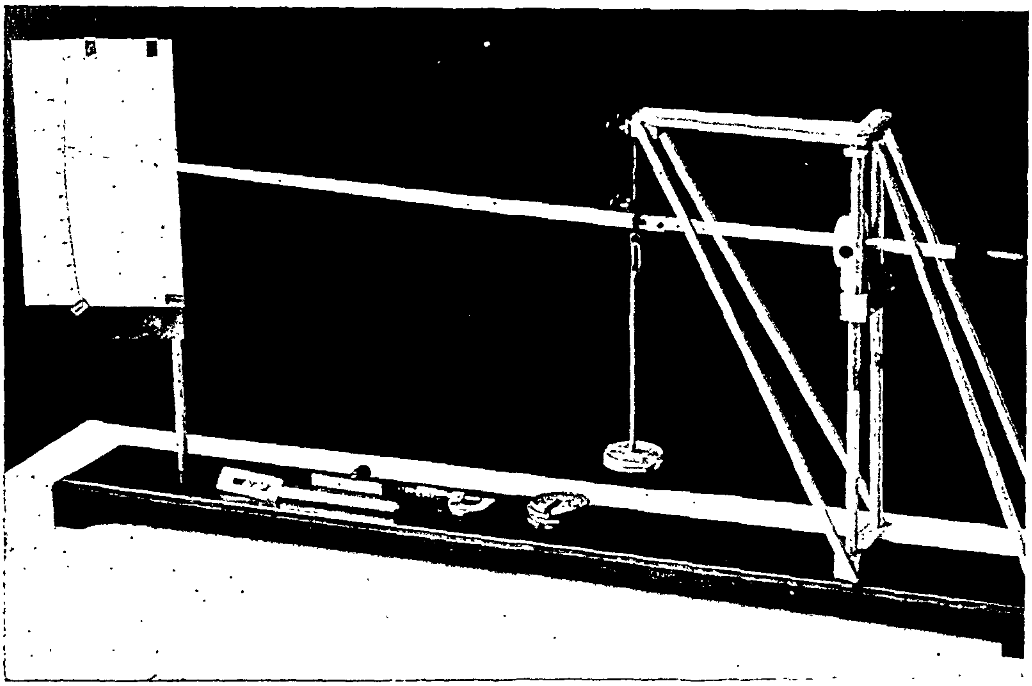

Fig. 1.—Apparatus for determining elasticity of tissue.

was cut out. An effort was made to avoid inclusion of calcified regions if such were present. The thickness of the strip obtained was measured in the middle and toward each end with a caliper micrometer; care was taken to close the calipers with uniform snugness, and each measurement was taken three times. The average of these three readings was taken as the thickness of the portion calibrated, and the average of the thicknesses of the three portions measured was taken as the thickness of the strip for purposes of comparison. The strip was then placed in the clamps of our apparatus, so that without weight applied the section of the strip between the clamps measured accurately 4 cm. Weights of 50 gm. each were then hung successively on the lower clamp. With the first weight and with each additional weight the strip was allowed to stretch for half a minute before a reading was made on a magnified scale. Six weights were used with each test, resulting in six readings for each strip. In making the tests we endeavored to minimize errors of personal equation by using exactly the same technic with all strips.

Fig. 1 is a photograph of the apparatus used, a brief description of which follows: On a rectangular wooden base board is mounted at one end a rigid *aluminium*

gallow and at the opposite end a vertical reading scale. At a properly selected point on the vertical portion of the gallow is constructed a fulcrum for an aluminium balancing bar with as little friction as is practicably possible. One arm of the bar extends in the form of a pointer toward the reading scale. Integral with this arm is a fastening clamp situated directly under a similar fastening clamp at the distal end of the horizontal portion of the gallow. On the arm, immediately beneath the clamp, is attached a ring to which the loads can be applied. Proper initial balance of the bar is secured by an adjustable counterweight on the opposite arm. The reading scale is adjusted in such a position that when the pointer is directed to the zero mark, at the upper end of the scale, the length of the strip of aorta between the two fastening clamps is exactly 4 cm. Direct determination of increasing distances between the clamps results in magnification of the scale, rendering the readings accurate to one-tenth of a millimeter.

The data concerning age, sex, average blood pressure, clinical history, cause of death and degree of visible arteriosclerosis of the aorta were recorded in each case. Arteriosclerosis was graded grossly by inspection of the entire aorta and the degree of sclerosis and the extent of the distribution were graded separately and then combined. This grading is naturally variable, depending on the discretion of the grader, but as far as possible it was done by the same person.

By plotting the results of the stretching on graph paper, using for abscissas the successive changes in weight, and for ordinates the corresponding increments of length, it was seen that the resulting line drawn formed a curve approaching the hyperbola without having the mathematic function of this figure. This result corroborated the work of previous investigators.[1, 4, 5, 8]

OBSERVATIONS

Relation of Elasticity to Age.—The results were plotted on graph paper for each weight used (50, 100, 150, 200, 250 and 300 gm.), the ages in years of the subjects being used as ordinates and the increments of length of the strips as abscissas. From the age of seven years to that of twenty-seven years there was an increase in extensibility, and after the age of twenty-seven years there was a steady decrease. There were, however, only seven instances in which the subjects were aged from seven to twenty-seven years inclusive. The results with strips from subjects aged more than twenty-seven years grouped themselves fairly closely about a straight line. The greatest spread occurred with the smallest weight applied, 50 gm. The increase in extensibility before the age of twenty-seven years was more rapid than the decrease after that age. Figure 2 is a graph of the result obtained when the figures recorded with the 100-gram weight were plotted.

Relation of Elasticity to Sex.—The results were next plotted on graph paper for each weight used in the same manner as in the preceding graphs, red dots representing females and black dots representing males. The red and black dots were so distributed that there appeared to be no difference in degree of extensibility with sex. This is opposed to the results of Herringham and Wills, who stated that at every age aortas of females are less elastic than those of males.

Relation of Elasticity to Blood Pressure.—For comparison the average of the diastolic blood pressures obtained while the subjects were in

hospital were used. The subjects were divided into age groups for the study of this feature as follows: ages seven to twenty-nine years inclusive, nine subjects; ages thirty to thirty-nine years inclusive, twelve subjects; ages forty to forty-nine years inclusive, thirteen subjects; ages fifty to fifty-nine years inclusive, twenty-two subjects; ages sixty to sixty-nine years inclusive, twenty-six subjects, and ages seventy years or more, eighteen subjects. This grouping was made in order to minimize the influence of age in this consideration. Within each of the age groups the subjects were arranged serially according to the height

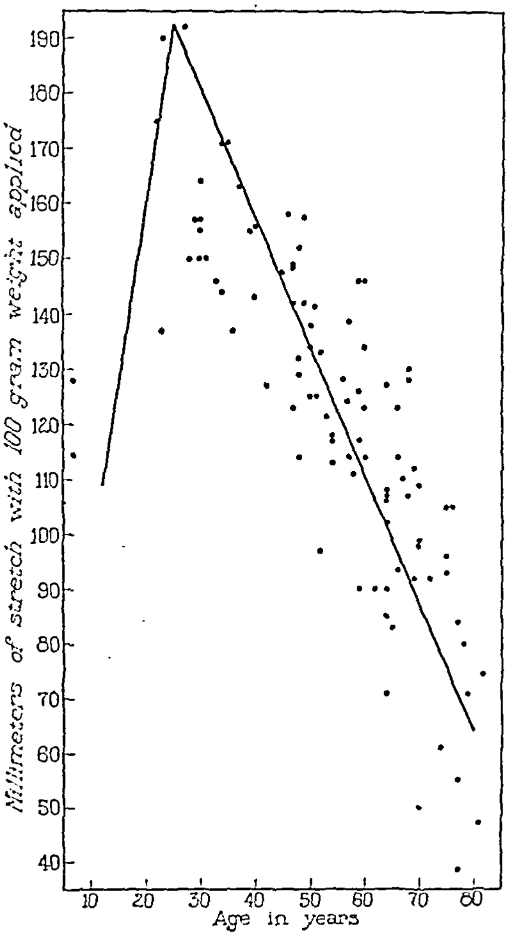

Fig. 2.—Relation of elasticity of strips of aorta to ages of subjects.

of the diastolic blood pressure. A study of this compilation did not reveal any relation between extensibility and diastolic blood pressure.

Relation of Elasticity to Degree and Extent of Arteriosclerosis of the Aorta.—In this study the subjects were arranged within each age group according to the classification of arteriosclerosis adopted, and the stretch of the strips with each weight was set down. In the age group thirty to thirty-nine years inclusive (twelve subjects) there was increased extensibility with increased amount of sclerosis, but in the other groups there was no apparent relation between extensibility and sclerosis. It

seems fair to conclude, therefore, that the elasticity of the aorta is not influenced parametrically by the sclerotic changes present, when the extensibility is determined of a strip of the aorta which is not involved in calcification. Calcification obviously would completely abolish elasticity.

Relation of Elasticity to Thickness of Wall of Aorta.—The results were plotted on graph paper for each weight applied, the abscissas used being the figures expressing the thickness of the strips as determined in the way already mentioned, and the ordinates used being the increments of stretch. The dots showed such a spread as to make it apparent that thickness does not play a part in the extensibility of the strip.

Relation of Elasticity to Clinical History and Cause of Death.—A relation was not apparent between extensibility and the nature of disease or diseases causing death.

SUMMARY AND CONCLUSIONS

An apparatus has been devised for measuring the extensibility of linear strips of the unembalmed aorta.

The extensibility of linear strips of 100 aortas of human beings was measured.

The curve drawn on graph paper, on which the results of these measurements were plotted, resembles a hyperbola without having the mathematical function of this figure.

The extensibility of linear strips of the aorta increases from childhood to the age of twenty-seven years. After the age of twenty-seven years it steadily decreases, irrespective of sex, diastolic blood pressure, degree and extent of grossly estimated arteriosclerosis (calcified areas being excluded), thickness of the wall of the aorta and cause or causes of death.

These facts do not necessarily mean that the elasticity of the aorta as a whole is greater in young adulthood than in childhood, because the linear strips used were all of the same size, and we did not consider the ratio of the size of the strip either to the circumference of the aorta or to its total area. The best way to determine the elasticity of the aorta as a functioning structure would be by studying the properties of internal pressure. Such an investigation would involve the variables of blood pressure, volume output of the heart per beat and total volume of blood at various ages; this would be extremely difficult and complicated. However, after physical maturity has been reached, these variables as well as the change in the size of the aorta, are not so pronounced from young adulthood to old age. Therefore the results obtained in this investigation might be applied to the elasticity of the aorta as a whole after maturity, if it were not for the fact that areas of calcification have been eliminated in the strips used; these would

necessarily affect the elasticity of the aorta as a whole. The conclusions reached from this study apply only to linear strips of standard size which do not contain regions of calcification.

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POLYPOID FIBROMA OF THE LEFT AURICLE (SO-CALLED CARDIAC MYXOMA) CAUSING A BALL-VALVE ACTION

WITH REPORT OF A CASE*

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MEDICAL literature contains a fair number of case reports of primary cardiac tumors designated as myxomas. The large majority of these rare tumors have been located in the auricles, the left auricle having been a far more frequent site than the right auricle. Of all the primary cardiac tumors, myxomas (so-called) are the most common. The literature, as reviewed by Karrenstein,[1] Nowicki,[2] Perlstein,[3] Beck and Thatcher,[4] Goldstein,[5] and more recently by Bradley and Maxwell,[6] contains less than seventy-five reports of tumors of this type. The following case is reported in the hope that the clinical observations and pathologic findings, when added to the previous contributions may be of value in working out some means of ante-mortem diagnosis.

CASE REPORT

The patient (Med. No. 33379) a white, Canadian-born housewife of forty-four years, entered the Medical Service of the Peter Bent Brigham Hospital as an ambulance case. Her chief complaint was of fainting attacks. The family history was not remarkable and gave no evidence of cardiac or of neoplastic disease. Her habits were of interest in that she was quite active for a woman of her age and swam a great deal. There had been several attacks of tonsillitis during the third decade. There was no history of previous circulatory symptoms, heart disease or of rheumatic fever. In the six weeks preceding entry there had been a loss of weight amounting to thirteen pounds.

The patient was quite definite in stating that she felt well and strong until six weeks before entry. At this time she experienced a moderately severe upper respiratory infection which, however, did not cause her to go to bed. In addition to a cough and yellowish sputum she noted rather marked substernal pain associated with her respiratory movements. Following recovery and during the fifth week before admission she resumed her swimming, and fainted for the first time upon coming out of the water. Somewhat alarmed, she stopped her housework and rested at home, but felt no need of going to bed. During the next four weeks she fainted four times and it was noted that each attack occurred while she was standing. It was known that her teeth needed attention, and three were extracted at home. Fainting did not occur again.

One week before admission moderate dyspnea developed and edema of the ankles was noted. The appetite, previously excellent, became poor; there were frequent dull frontal headaches and there was a marked increase in the urinary output. The patient had been in bed for four days when first seen; during this period the dyspnea and edema had increased, and cyanosis of the lips and finger nails appeared.

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She became definitely orthopneic and complained of her extremities feeling cold. Treatment during this last week had consisted of bromides and of an unknown quantity of digitalis given by a local physician.

Physical examination shortly after entry revealed a well-developed and well-nourished woman of middle age with only moderate dyspnea, orthopnea and cyanosis. She complained of persistent nausea and vomited twice during the examination. The rectal temperature was 101° F., pulse 110, respirations 30 per minute. The skin was warm, moist and clear. The eyes were quite normal. Ophthalmoscopic examination revealed no changes in the retinal arteries. The radial pulses were equal, synchronous, weak, and of normal rhythm. The vessel walls were elastic. The blood pressure, in the sitting position, was 65 mm. systolic, 57 mm. diastolic.

The apex impulse of the heart was felt, but not seen, 9.5 cm. to the left of the midsternal line in the fifth interspace and was forceful and sharply localized. Over this area there was a definite systolic thrill, remarkable in that it was only palpable over an area approximately 3.5 cm. in diameter. The heart was but slightly en-

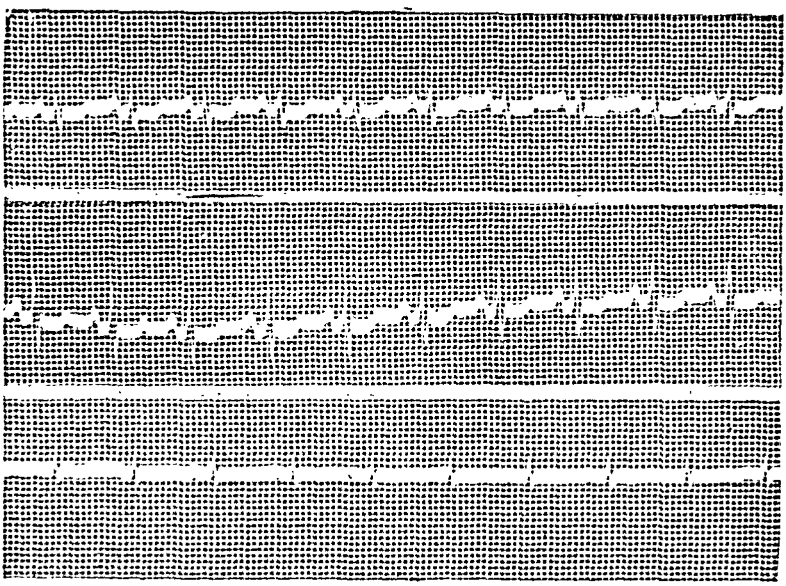

Fig. 1.—Electrocardiographic tracing from the three customary leads taken Sept. 27, 1928. Rate 120. The electromotive force is somewhat low.

larged, the left border of dulness being 10.5 cm. to the left of the midsternal line in the fifth interspace, and the right border of dulness 2.5 cm. to the right. A soft systolic murmur was heard at the apex, together with a short presystolic rumble which did not obscure the first sound. There was no suggestion of gallop rhythm.

The lungs were resonant, except at the posterior bases where there was slight dulness, this being more marked on the left. The breath sounds were vesicular throughout, but were noted to be somewhat distant over the left base. Tactile fremitus was slightly diminished over the same area. There was no alteration in the transmission of the spoken and whispered voice sounds. A few fine crackling râles were heard over both lung bases. The liver was palpable 3 cm. below the right costal margin and was rounded, smooth and quite tender, but did not pulsate. The hands and fingers were cyanotic and cold. The legs showed marked pitting edema extending up to the knees. Moderate sacral edema was also present.

Only one specimen of urine was examined, this being light straw in color, alkaline, and containing no albumin or sugar. Only a few leucocytes were seen in the sediment. Examination of the blood showed a hemoglobin value of 80 per cent (Tallqvist); red cells 5,510,000 and white cells 21,400 per c.mm. The stained smear

gave the appearance of very slight central achromia and of a normal number of platelets. Polymorphonuclears 74 per cent, lymphocytes 20 per cent, large mononuclears 4 per cent, undetermined 2 per cent. An electrocardiogram taken three hours after entry showed a sinus tachycardia, rate 120. (See Fig. 1.) There was a somewhat abnormal form of ventricular complex and the appearance of moderately

Fig. 2.—A photograph of the opened heart fixed in Kaiserling's solution, showing the position of the tumor mass.

Fig. 3.—A photograph of the fixed specimen with tumor lifted above the mitral valve, showing the pedicle attachment.

low electromotive force. There was no evidence of digitalis intoxication. The blood Wassermann was weakly positive. The Hinton precipitin test for syphilis performed upon the same serum was negative.

On the basis of the above findings, the diagnosis of mitral stenosis and congestive heart failure was made, and the patient was placed upon the Karrell diet and given

morphine. In view of the vomiting and of the history of digitalis having been taken just before entry, a total of only 0.3 grams of digitalis leaf was given during the afternoon. Under the rest and morphine her temperature, pulse and respirations all became lower and her condition seemed greatly improved. There was some vomiting about 6:00 P.M. Within eight hours after admission the temperature had fallen to normal, the pulse from 110 to 95, and respirations to 20.

When seen at 12:30 A.M. the night of admission the patient was sleeping quietly, being propped up on her back rest and pillows. The respirations were slow, regular and normal in type. The pulse was improved in volume, quite regular, rate 90. She was not awakened and the blood pressure was not taken. The patient continued to sleep for the next three hours and the night nurse found her condition unchanged at 3:20 A.M. At 3:30 A.M. she was found dead, her position upon the pillows being unchanged. This was fifteen hours after admission.

Necropsy.—An examination of the body, limited to the thoracic viscera, was performed seven hours post-mortem. The body was well developed and well nourished.

Fig. 4.—A photograph of the fresh specimen. Note peculiar color value of tumor, which was semitranslucent and yellowish.

Moderate pitting edema was present on the legs below the level of the knees. Rigor mortis was present to a very slight degree and post-mortem lividity was prominent over the back, thorax and neck. The lips and ears were very cyanotic.

When the sternum and adjacent ribs were removed the left pleural cavity was found to contain 700 c.c. of clear straw-colored fluid. The right pleural cavity was entirely obliterated by dense fibrous adhesions between the visceral and parietal pleurae. The heart was displaced slightly to the left.

The pericardial cavity contained about 20 c.c. of clear straw-colored liquid. There was, however, a purplish hemorrhagic discoloration beneath the epicardium over the right auricle, obviously due to slight extravasation of blood. The pulmonary arteries opened in situ were entirely normal. The heart, after removal and freeing of blood clots, weighed 325 grams. The valve measurements were all within normal limits, T.V. 11 cm.; M.V. 10 cm.; P.V. 6.5 cm. The aortic valve was not opened as it showed no abnormality when examined from above or below. Examination of the various segments of all of the valves showed no evidence of vegetations, and there

was no thickening or scarring to suggest previous valvular injury. The myocardium of the left ventricle measured 11 mm. in thickness, and the right ventricle, which was somewhat hypertrophied, measured 5 mm. in thickness. There was no evidence of gross scarring in the myocardium on various section planes and all of the chambers were free of thrombi. On opening the left auricle, a tumor mass was found almost filling the otherwise empty cavity. This tumor consisted of a lobulated, poly-

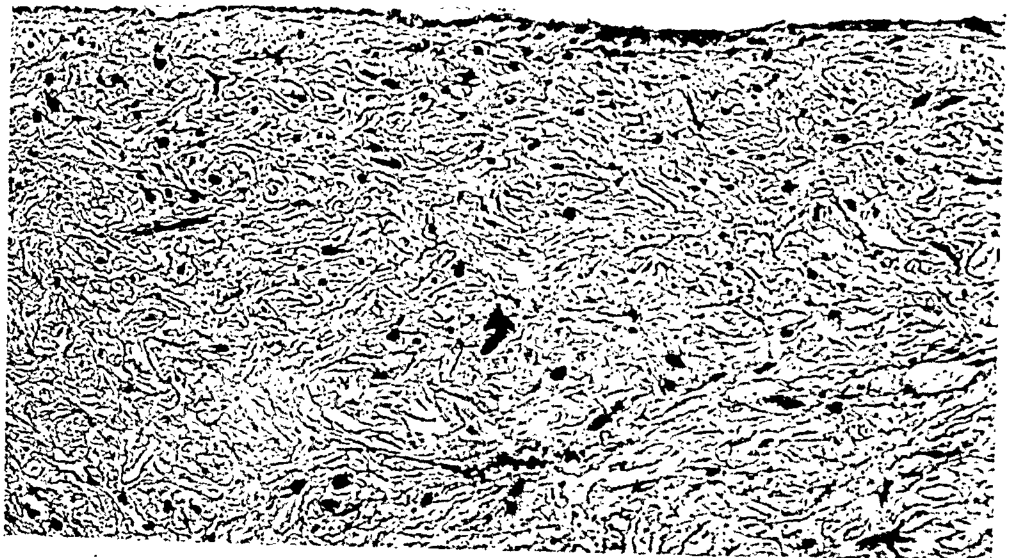

Fig. 5.—A low power photomicrograph showing a cellular border of the tumor, a fibrillary and granular matrix, fusiform and stellate cells and the elastic tissue fibrils. (Section stained with anilin blue.)

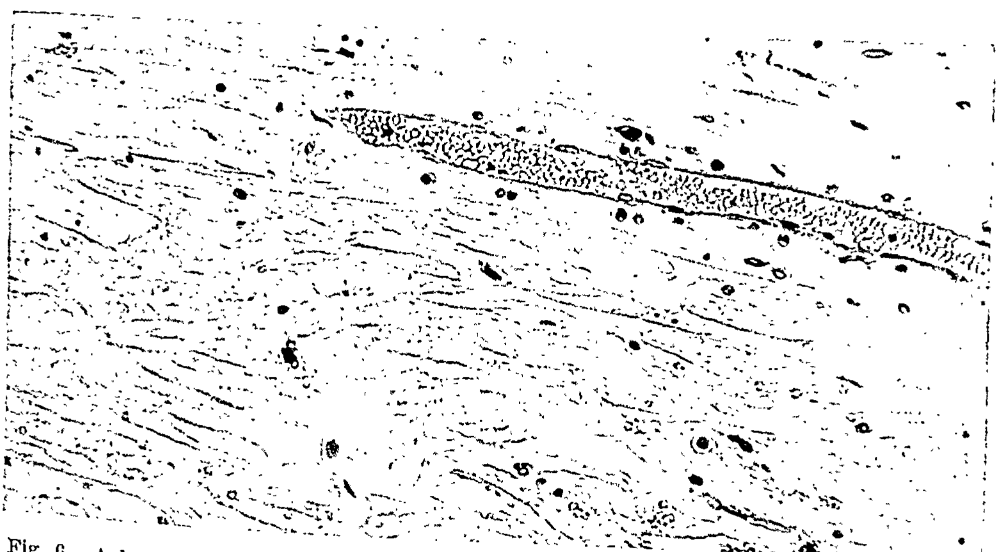

Fig. 6.—A low power photomicrograph showing the scarcity of cells and the relative abundance of pale staining intercellular substance. (Section stained with hematoxylin and eosin.)

poid growth, the external surface of which was smooth and glistening. In color it was pale yellow and on the fresh cut surface was soft, translucent and gelatinous. The only attachment to the auricular wall was by way of a dense fibrous pedicle measuring 5 mm. in diameter, which was firmly attached to the interauricular septum 11 mm. above the free margin of the mitral valve and about 8 mm. below a small perforate foramen ovale. The surface made by an incision through the interauricular septum from the right auricle showed the fibrous tissue of the pedicle to extend through one-half the diameter of the septum and to spread upward and downward in a fan-shaped manner.

The tumor measured 4.5 cm. by 4 cm. by 3 cm. in its greatest dimensions. When first seen, the polypoid growth rested snugly in the mitral valve, but it could be moved freely upon its pedicle and could be displaced well above the base of the valve segments. While fresh, the tumor appeared edematous; it was soft and jelly-like. Small snippings of the tumor when placed on a glass slide and examined microscopically were found to contain oval, fusiform and stellate connective tissue cells, in an abundance of transparent intercellular material. There were no areas in the gross to suggest thrombus formation.

Microscopic Examination of the Tumor.—Sections from the various portions of the tumor were stained by the following methods: eosin methylene blue, mucicarmine, phosphotungstic acid haematoxylin (Mallory), elastic tissue (Weigert), anilin blue (Mallory) and by Levaditi's method for the demonstration of spirochetes.

Paraffin sections stained with eosin methylene blue revealed a tumor which was poor in cells. The intercellular matrix or background in these preparations was uniform, stained faintly and was traversed by a fair number of thin-walled, small blood vessels and a few capillaries. In the anilin-blue preparations the background was resolved into blue-staining fibrils between which a finely granular, reddish brown material was incorporated. The phosphotungstic acid haematoxylin stain brought out the same type of intercellular material as a light brown, granular substance between more definite red brown, collagen fibrils. Occasional wavy elastic fibrils were seen in the sections stained by Weigert's elastic tissue method. None of the sections stained by appropriate methods gave typical mucin reactions. In general, the cells were elongated and fusiform in shape, though there were branching and stellate forms like those of embryonic connective tissue. The cells of the tumor were arranged either singly or in small groups and cords of from two to six cells each. In many instances there were small cell clusters about which a condensation of collagen had occurred. Excepting the fusiform and branching forms, the majority of cells were small, oval or round with a scant rim of cytoplasm surrounding a prominent and good sized nucleus.

No definite architectural detail could be made out except at the very periphery where the collagen was very dense with fibrils running parallel to the surface. The surface of the tissue was covered in part by flattened or oval cells, entirely similar to those cells found in the substance of the tumor. Occasional fusiform or stellate shaped surface cells showed cytoplasmic extensions into the underlying intercellular matrix.

Sections from near the tumor pedicle showed a small area, 4 mm. in diameter, in which there were numerous phagocytic cells, laden with hemosiderin granules. No other such areas were found in sections from other portions of the tumor. In the pedicle of the tumor there was marked condensation of the collagen into dense interlacing bundles. Examination of sections from representative blocks stained by Leviditi's method for the demonstration of spirochetes proved entirely negative.

DISCUSSION

A few authors, notably Warthin,[7] have felt that cardiac myxomas were not true neoplasms but that in reality they represented degenerating forms of organized thrombi. Warthin found intramural mucoid nodules of the heart in congenital syphilis, the nodules of which resembled mucoid tissue and gave positive mucin reactions. In these myocardial lesions he was able to demonstrate colonization of Spirocheta pallida. These lesions, together with the finding of mucous-like connective tissue in organizing thrombi and in the early stages of organizing valvular vegetations, caused him to conclude that the entire group of reported cardiac myxomata should be rejected as myxoblastomas.

Wells,[8] on the other hand, has felt that many of the so-called myxomas are in reality edematous fibromas or polypoid tumors, in which the resemblance to true myxoma is more structural than chemical. He further states that this form of mucoid degeneration seems to be a reversion to the fetal type of connective tissue, which is characterized, as in the umbilical cord, by an excessive accumulation of a mucin-containing fluid intercellular substance and a paucity of collagenous fibrils.

We have had no hesitancy from the first in considering the present specimen as a true tumor composed of a fetal type of connective tissue and hence myxomatous in appearance. We also have concluded that many of the reported cases were so remarkably similar that they also should be placed among the true connective tissue tumors. The present tumor was found attached to and embedded in the wall of the left auricle by a dense connective tissue pedicle. The surrounding endocardium as well as the lining of all the chambers of the heart showed no evidence of scarring or active inflammation, and there were no thrombi. We have found no reports of single vegetations or solitary thrombi arising from the interauricular septum, in otherwise normal hearts. Norton[9] found that according to reported cases, 75 per cent of the so-called cardiac myxomas occurred in the left auricle. Granting that organizing thrombi and vegetations with early organization may show embryonic or mucous connective tissue, there should be portions of these large tumors which would show remnants of the original thrombus. Scattered groups of hemosiderin-filled phagocytes would not be conclusive evidence of thrombus origin, since small focal hemorrhages in pedunculated tumors would be likely to occur subsequent to minor strangulation or tortions. A thrombus would be expected to show evidence of layer formation and to be more dense in the central portion. The present tumor was uniform throughout, being pale yellow, translucent and gelatinous. It should also be emphasized that it had a smooth, though lobulated, and glistening external surface with no attached blood clot. Histologically the cellular elements were mostly those of embryonic connective tissue, the intercellular substance was mucinous in structure, elastic fibrils were numerous, and there were a fair number of orderly arranged blood vessels. Ewing[10] states that primary sarcomas of the heart are probably connected in origin with the myxomas. He also refers to the possible origin of myxomas in the superfluous embryonal tissue in the region of the foramen ovale, where so many of these growths have been attached.

In view of the pathological findings, an analysis of the mechanism producing the presenting symptoms is of interest. The rapid onset of symptoms in an adult, who has always been well, would necessitate either a rapid enlargement of the tumor or some alteration in position to produce the signs of valvular disease. Rapid enlargement of a tumor of this type could occur through edema or hemorrhage, the latter changes resulting from partial or complete obstruction of the blood vessels of

the pedicle by torsion. With the enlargement of the tumor, the auricular cavity would be taken up by the neoplasm so that insufficient space would be available for proper circulatory function. Valvular stenosis and insufficiency are possible when, as in this case, the tumor arises from a valve segment or when the pedicle is sufficiently long to allow the growth to project into the valve orifice. Pavlowsky[11] observed in the case reported by him that when the patient was lying down, there were signs of mitral insufficiency; when in a sitting posture there were signs of mitral stenosis, with much greater distress to the patient. These relationships were confirmed by similar positions at necropsy.

Our informant denied the occurrence of any convulsive or epileptiform movements, although such seizures are probably the most frequent presenting symptom in this type of cardiac tumor. A striking feature of the history, however, was the occurrence of five sudden attacks of fainting. Each of these attacks occurred while the patient was in the standing position. It seems possible that the fainting could have been caused by the pedunculated tumor dropping into and partially or completely blocking the mitral orifice. The subsequent fall to the horizontal position may have dislodged it. We feel with Weltmann[12] that the above mechanism may at times suggest the Adams-Stokes syndrome.

SUMMARY

1. A case of intracardiac tumor arising from the interauricular septum is reported and illustrated by gross and microscopic photographs.

2. We have found no record of this condition ever having been diagnosed before necropsy.

3. A tumor of this type may produce a ball-valve action in every way similar to the action of a ball thrombus.

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ANEURYSMS OF THE BRONCHIAL ARTERIES*

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ANEURYSMS have been described in many arteries. They have been found involving nearly every part of the arterial system from the sinus of Valsalva to the smaller peripheral arteries of the brain, abdominal viscera, and the extremities. A careful search of the literature fails to disclose any reference to aneurysm formation of the bronchial arteries, a case of which came to my attention at the Harlem Hospital.

These arteries, one right and two left, usually arise from the anterior wall of the thoracic aorta just above the level of origin of the intercostal arteries. Frequently the right and occasionally the left arteries arise from the upper aortic intercostal arteries as small branches of these vessels or by a common stem. In the case reported, these vessels arose directly from the aorta, in line with the intercostal arteries. There were twelve such pairs, all arising from the posterior aortic wall; from the anterior wall, no branches arose. The lower nine pairs of arteries were distributed to the intercostal spaces; the upper three ran in the direction of the bronchi.

CASE REPORT

J. C., aged thirty-five years, colored male, was admitted to the Harlem Hospital, in a semistuporous condition. The meager history obtained from his brother was that he had apparently been well until two days before admission when he developed an unproductive cough and experienced difficulty in breathing. Patient had difficulty both on inspiration and expiration, his breathing being of a "crowing" nature. The cough and dyspnea became more severe. On the day of admission he seemed dazed, his speech incoherent. No other symptoms were present, nor did his brother think there had been any fever.

While in the admitting room (where he had been sent by his physician as a diphtheria suspect) he suddenly became very cyanotic and lapsed into coma. Tracheotomy was performed, a tube inserted into the trachea in the midline immediately below the larynx, without relief of his symptoms.

Physical examination (in the ward) disclosed a well-developed and nourished young colored adult male, breathing in a very labored manner. Skin was cold, rather clammy. Corneal reflexes were active; pupils in mid-dilatation, equal, and reacting sluggishly to light. Ears, nose and mouth were negative. Tracheotomy tube was present in the midline of the trachea, below the larynx. Heart seemed pushed to the right, the right border being in the midclavicular line, the left border at the left sternal border. The cardiac dullness area in the first interspace meas-

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ured 4 inches in width, equally to the right and left of the midline. Heart sounds were faint and distant but were heard throughout the entire anterior chest; no murmurs; A_2 accentuated.

Lungs showed no impairment of resonance. Breath sounds were faint and distant; no râles present. Suprasternal and substernal retraction of chest marked.

Abdomen, extremities and reflexes were negative.

Blood pressure on the two arms showed systolic 90 mm., diastolic 50 mm. on the right, and systolic 106 mm., diastolic 60 mm. on the left.

Fig. 1.—Anterior view of heart and aorta showing openings of aneurysms in line of lateral intercostal arteries, and displacement of left subclavian and carotid arteries to right.
1, Left common carotid; *2*, *3*, *4*, openings of aneurysms.

Temperature on admission 100°; pulse 76 and regular, unequal, right stronger than left; respirations 20, shallow and very labored. Four hours later (just preagonal) temperature was 100.2°; pulse 96; respirations 32.

Blood count showed R.B.C. 3,800,000; Hgb. 70 per cent (Sahli); W.B.C. 13,000; polynuclears 77 per cent; lymphocytes 21 per cent; transitionals 2 per cent.

Urine showed a trace of albumin, a few hyaline and granular casts, and an occasional erythrocyte.

The coma deepened, the obstructive breathing became more labored and shallower. Generalized twitches of the entire body appeared. Death supervened four hours after admission.

AUTOPSY REPORT

Body is that of a well-developed and nourished young male negro, 68 inches in length. Two-inch midline tracheotomy incision beginning immediately beneath lower border of thyroid cartilage.

Neck organs not grossly remarkable.

Chest: On opening the chest, a large mass rises from above the first portion of the descending aorta, just beyond the left subclavian artery, and projects upward to the superior aperture of the chest. The left subclavian artery is pushed to the right; its lumen narrowed, measuring 0.5 cm. at its origin and for 2.5 cm. of its

Fig. 2.—Posterior view of aneurysmal mass to show relation to trachea, left bronchus, and esophagus (held by glass rods) and posterior view of aneurysmal openings.

1, Upper end of mass; *2*, *3*, *4*, openings of aneurysms (filled with blood clot); *5*, left main bronchus; *6*, esophagus; *7*, lower end of mass.

course, where it winds anteriorly to and above the mass in its course to the axilla, its lumen then widening to 1.2 cm. The mass measures 6 x 10 x 5 cm. It extends downward along and behind the descending thoracic aorta to the level of the fourth intercostal arteries. Posteriorly it extends behind the aorta, left subclavian and left common carotid arteries. It compresses the esophagus and trachea, completely occluding the esophagus and left stem bronchus at its origin. At the bifurcation, the tracheal lumen is very markedly narrowed, barely admitting a probe 0.2 cm. in diameter.

The outer upper surface of this mass is intact, very thin; beneath it a firm blood clot is visible. The posterior surface was torn across in removing the speci-

men. It presents three distinct openings respectively from above downward 3, 2, and 1 cm. in diameter, filled with clotted blood. These openings are separated from each other by narrow bands of tissue continuous with the surface covering.

On opening the aorta, in the line of the lateral intercostal arterial mouths, are three large openings, respectively 1, 2, and 0.6 cm. in diameter from above downward. Corresponding to these openings are three minute openings in the line of the medial intercostal arterial mouths. The large openings lead directly into the blood-clot-filled mass described. When the clots are evacuated, the mass appears as three wide noncommunicating tubes, each about 4 cm. in length. The wall of each is thin, the inner surface eroded and without any intima. The wall of the aorta at the site of the openings and in various portions of the ascending arch and descending aorta measures uniformly 0.4 cm. in thickness; that of the tubes is paper thin. Its wall is directly continuous with the aortic wall. The course of the lower nine intercostal arteries can be traced from their origin well under the ribs; that of the first three lateral arteries is lost in the mass, being demonstrable for only a short distance near the esophagus and left bronchus.

The intima of the aorta contains numerous small yellowish atheromatous plaques and innumerable fine longitudinal striations. Around these striations the intima is of a light brown color. The aorta is quite inelastic. The striations are most numerous in the sinuses of Valsalva and in the arch and descending aorta near and between the large openings described, where the intima is markedly puckered.

The heart is relatively small, weighs 165 gm. Pericardium smooth, glistening; no fluid present in sac. Myocardium firm, not thickened; papillary muscles not thickened, chordae tendineae not shortened. Aortic valve cusps definitely thickened along line of attachment where a few small atheromata are present; remainder of valve and other valve cusps are thin and translucent. Aortic cusps were retracted from coronary arteries.

MEASUREMENTS

Thickness left ventricle	2.0 cm.
Thickness right ventricle	0.4 cm.
Circumference aortic valve	6.0 cm.
Circumference mitral valve	7.2 cm.
Circumference pulmonary valve	8.0 cm.
Circumference tricuspid valve	11.2 cm.

All the pulmonary lobes were markedly emphysematous, collapsing somewhat when the heart and mass were removed. Abdominal organs not noteworthy.

MICROSCOPIC EXAMINATION

1. Sections of the arch and descending portion of aorta showed marked lymphocytic and plasma-celled perivascular infiltration of the vasa vasorum and fragmentation of the medial elastic tissue fibers. The intima showed some endothelial proliferation and numerous collections of needle-like cholesterin crystals in the subendothelial tissue. The inner elastic lamella was intact.

2. Sections of the wall of the aneurysmal sacs showed the intimal lining present in but a few places; the inner elastic lamella and the medial elastic tissue are markedly fragmented, numerous very short, frayed fragments being apparent in the fibromuscular tissue of the wall which is rather densely infiltrated with lymphocytes. A few small arterioles, near the outer edge of the wall, show a marked perivascular zone of lymphocytes. No spirochetes demonstrable (Levaditi stain).

3. Sections of the first four intercostal arteries and proximal three centimeters of innominate, left carotid and subclavian arteries showed a picture similar to that

in the aorta. Sections of other portions of the carotid arteries, the iliacs, and proximal two centimeters of the hepatic and superior mesenteric arteries showed a slight perivascular lymphocytic infiltration of the vasa vasorum; no elastic fiber fragmentation was present. A few of these vasa vasorum showed marked prolifera-tion of the intima and narrowing of the arterial lumen. No hyalinization or cal-cification of the wall, nor thrombi in the lumen, or ulceration of the intimal surface was present. The other vessels showed the intimal proliferation to a less marked degree.

Sections of other arteries (renals, splenic, inferior mesenteric, pulmonary) showed an occasional adventitial vas vasorum surrounded by a narrow, usually single-celled, layer of lymphocytes. In these sections an occasional vas vasorum showed a slight degree of intimal proliferation.

4. Sections of the heart (interventricular septum, near base, and right and left ventricular walls) show small areas of fibrous tissue irregularly distributed between the muscle fibers, fading indefinably into the finer intermuscular reticular tissue, and only here and there apparently close to a blood vessel. The intima of the larger arterioles is moderately proliferated; no cellular infiltration of the wall is present.

5. Sections of the other organs show no noteworthy changes.

DISCUSSION

Aneurysms of the smaller arteries have been described in the brain,[1] coronary,[2] hepatic,[3] renal,[4] gluteal,[5] popliteal and posterior tibial[6] arteries. These are seldom of syphylitic origin. Thus the very infrequent renal arterial aneurysmal dilatations described were multiple, generally at the hilus or in the adjacent parenchyma, and varied from the size of a walnut to that of a child's head. They were generally caused by perivascular (intraperitoneal) inflammatory lesions;[7] tuberculosis[3] and atherosclerosis and trauma[8] have also been reported as etiologic factors.

Syphilis as a cause of aneurysms of the smaller arteries seems rather infrequently mentioned. In fact, even in the aorta, luetic aneurysms appear hardly more frequently than aneurysms of arteriosclerotic non-luetic origin. According to Berger,[1] even at the base of the brain where the smaller arteries more frequently present aneurysms than elsewhere among arteries of similar size, not more than 10 per cent are syphilitic in origin.

In the case reported the luetic basis of the aneurysms was unquestioned, on histologic grounds. It is furthermore interesting to noté the extensive mesaortitis of other smaller arteries not showing aneurysms. This rather extensive involvement of the medium-sized arteries was very recently stressed by Saphir[9] who, in a study of fifty cases of syphilitic aortitis, found syphilitic changes in the innominate artery in thirty-three cases, in the carotid in twenty-nine, in the superior mesenteric and common iliacs in ten, in the inferior mesenteric in three and the femoral artery in seven cases. The early changes observed by him were characterized by an endarteritis of the vasa vasorum and a perivascular infiltration of lymphocytes in the adventitia. These early histologic evidences of syphilitic involvement occurred in our case in

the distal portions of the common carotid and common iliac arteries and the proximal 2 cm. of the hepatic and superior mesenteric arteries. In the renal, splenic, inferior mesenteric and pulmonary arteries similar involvement of the vasa vasorum and adventitia was present but to a far lesser extent. In the innominate, proximal part of the left common carotid and the left subclavian arteries evidence of a more advanced process was present in the form of fragmentation of the elastic fibers and interruption of the elastic lamellae. These latter changes were also apparent in the wall of the aorta, of the aneurysmal sac, and the first four intercostal arteries.

It appears that this was a case in which a very extensive syphilitic involvement of the arteries of all three sizes had occurred. The lesions were most pronounced and of longest duration in the arteries of the first and some of the third magnitude (bronchial and intercostal arteries). It appears not unlikely that those of the latter category not having a bony or surrounding muscular protective wall—the first three intercostal arteries, the bronchial arteries—formed aneurysms; these sacs in turn, by their external pressure perhaps preventing similar aneurysmal formation from the thicker walled aorta. The other intercostal arteries, although apparently as markedly involved in the syphilitic process but surrounded by firm supporting structures, did not form aneurysms.

SUMMARY

1. A case of multiple, saccular aneurysms of the bronchial arteries is reported, the first recorded in the literature. Death resulted from asphyxia caused by tracheal occlusion by the aneurysm.

2. The etiology is shown definitely to be luetic, a rather unusual finding in aneurysms of smaller arteries. Many other small and several medium-sized arteries showed syphilitic involvement varying from the early lesions of endarteritis of the vasa vasorum and lymphocytic perivascular infiltration of the adventitia to extensive destruction of the elastic lamellae.

3. The rôle of the supporting external structures in the formation of the aneurysms of the intercostal arteries and aorta in this case is indicated.

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"PLATEAU R-T" IN A CASE OF LOBAR PNEUMONIA*

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DURING the past ten years, a good deal has been said regarding an electrocardiogram which is characteristic of coronary artery disease. Rothschild, Mann and Oppenheimer,[1] Pardee,[2, 3] and Parkinson and Bedford[4] have all described a change which appears soon after the occurrence of coronary occlusion as well as the so-called "coronary T-wave" or "cove-plane T" which develops several days after such an accident. It is this first change in the ventricular complex in which we are particularly interested at present. This is designated by Parkinson and Bedford as the pleateau R-T and is universally described as a take-off of the T-wave from a point near the top of the R-wave on its downward limb. All of the above-named authors agree that this type of curve is characteristic of the early stages of coronary thrombosis.

This same type of electrocardiogram has been found in several other conditions: Kountz and Gruber[5] obtained it experimentally by producing anoxemia. They saw it in moderate degree after general anoxemia and after vago-pression. Scott, Feil, and Katz[6] reported it in cases of pericardial effusion which had come to autopsy and were known to have no coronary artery disease. De Graff and Wible[7] reported it after digitalis.

The present case is one of lobar pneumonia in which this plateau R-T was found during the routine examination of daily electrocardiograms taken as a part of the work on the study of digitalis in pneumonia.

The patient was a Mexican boy of twenty-two years who had been perfectly well until the acute onset of his present illness. Three days before entry he had a chill followed by fever, pain in the right upper chest, and cough with production of reddish brown sputum. He remained in bed most of the time before coming to the hospital and had no treatment other than cupping.

The family history was irrelevant, and the past history negative. His habits were good.

On entry, January 22, 1930, he was moderately cyanotic and dyspneic. The heart was not enlarged, the rate was regular, the sounds of good quality, and there were no murmurs. The blood pressure was 110/70 mm. In the right upper lobe

*From the Second (Cornell University) and Third (New York University) Medical Divisions of Bellevue Hospital.

anteriorly and posteriorly, the percussion note was dull, the breath sounds were bronchial with many crepitant râles, and the voice sounds were increased. Anteriorly, there was a definite pleural friction rub. Otherwise the lungs were clear. The diagnosis of pneumonia of the right upper lobe was substantiated by fluoroscopic examination.

The lung findings remained practically the same until January 31, when definite signs of resolution were noted. By February 3, these had disappeared and the lungs were entirely clear. The heart was examined daily and at all times the sounds were clear and of good quality. Never was a pericardial friction rub heard and never were any abnormal pulsations seen. The patient never admitted having any pain besides that in the right upper chest. Cyanosis was moderate at the time he entered and gradually decreased until January 27, when it was no longer noted. There was moderate dyspnea on admission but this had disappeared by the end of the fourth day, which was the fourth day before the temperature had dropped. There was no great prostration during the acute stage and there was less weakness following the illness than is usually found after pneumonia. The blood pressure

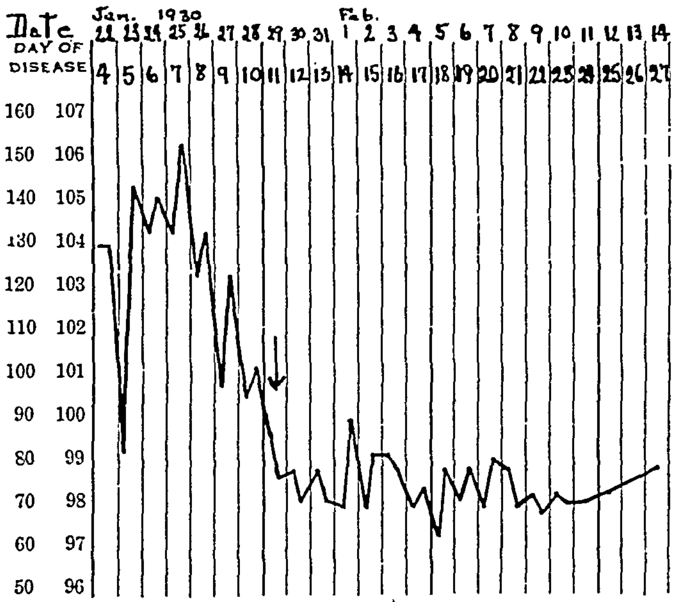

Fig. 1.—Temperature Chart. Arrow indicates date on which plateau T-wave first appeared. Note that the temperature curve at this time is dropping very rapidly.

was taken at short intervals and remained approximately the same as on admission. The urine was negative except for a trace of albumin. The sputum contained pneumococci type V. and the patient was treated during the febrile period with antipneumococcus serum mixed: types IV. V. and XIII.[8] At no time did he receive digitalis.

On the 11th of February, the patient was discharged in good condition. On the 14th, he returned for the customary reëxamination when there were no abnormal physical findings. On the same day, he was given an exercise tolerance test according to the method of Master and Oppenheimer[9] which gave him a rating of 26, the normal for his age, weight, height and sex, being 25.

The electrocardiographic findings are shown in the accompanying figures. It will be noted that although the point of origin of the T-wave on the R-wave began to rise during the febrile period, it reached its greatest height on January 29, when the temperature had dropped to 98.8 degrees. Since the temperature was normal when the T-wave showed the most marked plateau form, and since the cyanosis had disappeared even before this, we feel that the picture cannot be explained by

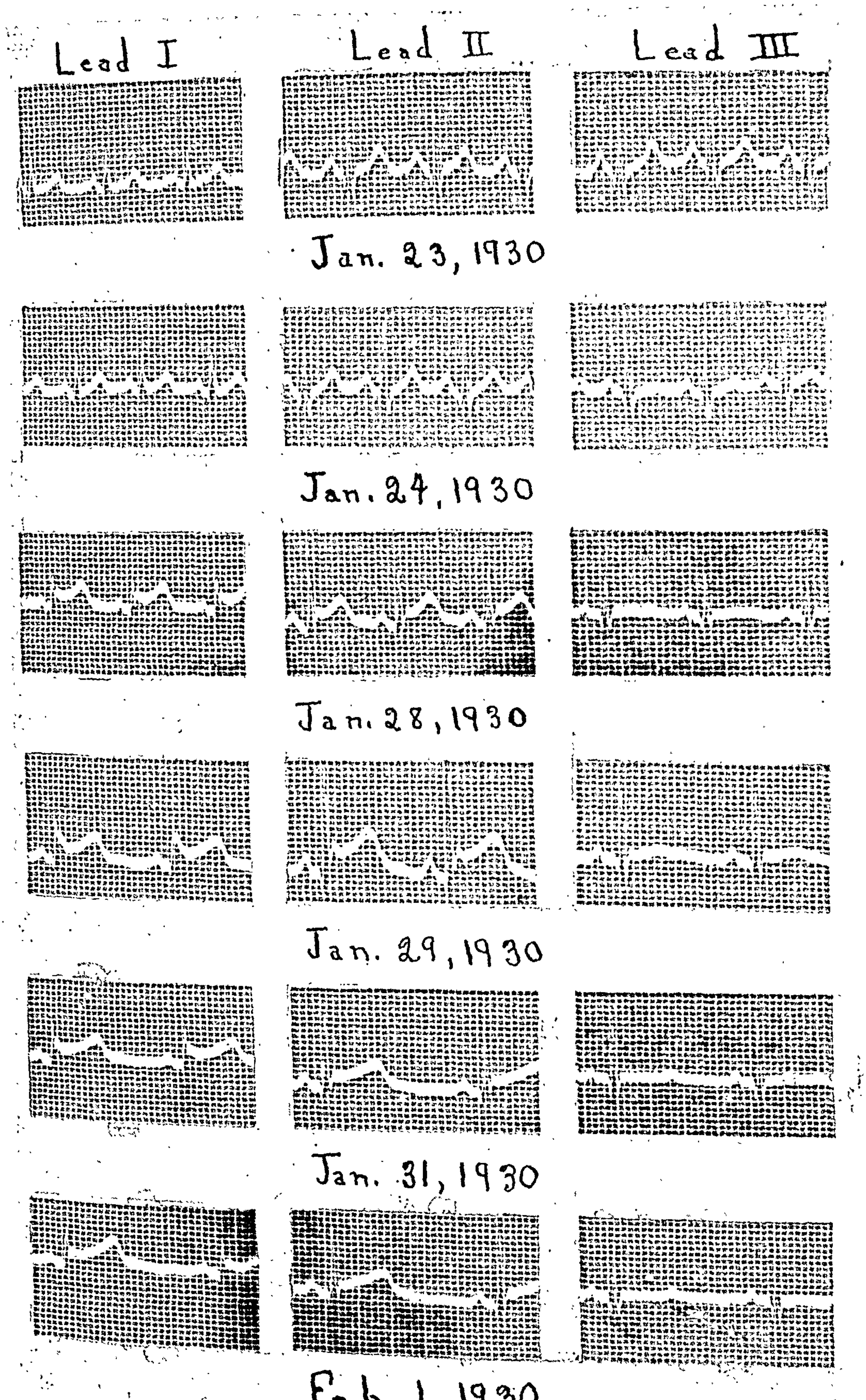

Fig. 24.—Successive changes in the electrocardiogram.

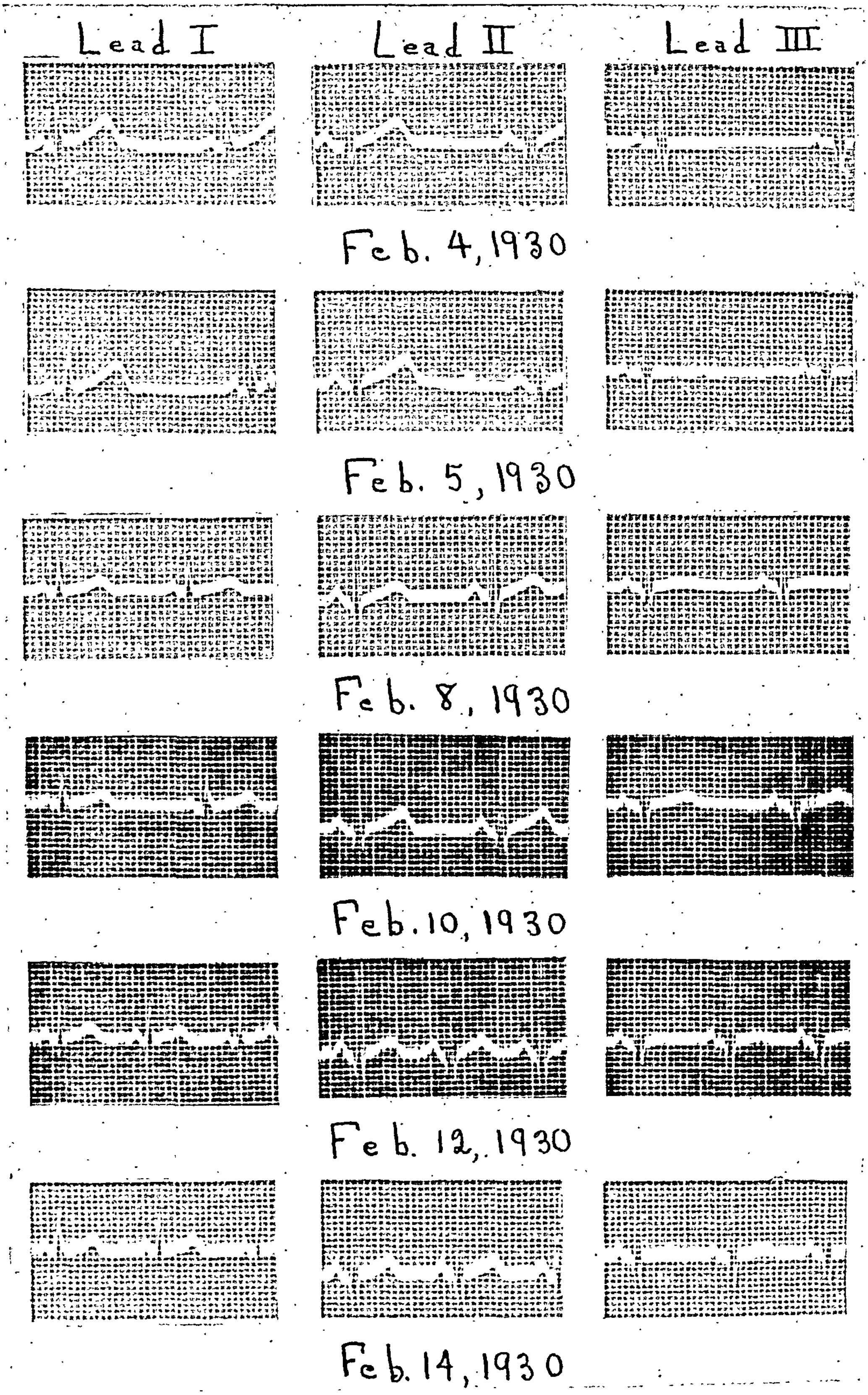

Fig. 2B.—Successive changes in the electrocardiogram.

anoxemia. It will also be seen that the S-T segment gradually returned to normal rather than developing into the phase of the cove-plane T. This transition, therefore, is different from that usually described as occurring during the course of coronary thrombosis. In view of this fact as well as that the patient recovered without any functional impairment of the heart, we are convinced that the S-T segment of these electrocardiograms must have some cause other than coronary artery disease, pericarditis, anoxemia, or digitalis. At the present time the exact cause is still in doubt. A possible explanation is toxic myocarditis, but there was nothing in the clinical picture to substantiate this.

SUMMARY

A case of lobar pneumonia is reported in which the electrocardiograms show a "plateau" or "high take-off" type of T-wave without clinical evidence of coronary artery disease.

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Department of Reviews and Abstracts

Selected Abstracts

Van Liere, E. J., and Crisler, George: The Influence of the Pericardium on Acute Cardiac Dilatation Produced by Vaginal Stimulation. Am. J. Physiol. **94:** 162, 1930.

In continuation of work done previously by the authors, a study has been made of the restraining influence which the pericardium might exert on the heart. Instead of anoxemia as used in the previous experiments, the authors used vagal stimulation to produce the acute cardiac dilatation. The extent of the cardiac dilatation was measured by x-ray plates. Dogs were used in the experiments. It was observed that animals with the pericardium incised showed a greater cardiac dilatation when the vagus was stimulated to cause cardiac standstill than do animals with the pericardium intact. In some of the animals the evidence of dilatation was slight, but in all the tendency was for the heart to become dilated. In animals without pericardiotomy there was no appreciable change following vagus stimulation.

The authors believe that the pericardium restrains excessive cardiac dilatation caused by vagal stimulation and that this is further evidence that the pericardium exerts a protective action on the heart in conditions of extreme stress.

Weese, H.: I. Digitalis Consumption and Digitalis Effect in Warmblooded Animals. Arch. f. exper. Path. u. Pharmakol. **135:** 228, 1928.

A few minutes after the intravenous injection of digitalis, the greater part of the digitalis has disappeared. It has not been known what happens to it. No *digitalis is found in defibrinated blood.* It is *not excreted in the intestine and* urine. The purpose of the investigation was to show where the digitalis was stored and destroyed. This was done on Starling's heart-lung preparation on cats. The preparation was perfused with cat's blood, in some cases diluted with Tyrode solution, against an arterial resistance of 80 to 100 mm. Hg. The venous pressure *was 8 to 10 cm. Water temperature was 38° C.* The glucosides which were tested were digitoxin, G. Strophanthin scillaren. The criterion of the digitalis effect was asystole of the heart.

THERAPEUTIC EFFECT

The effect of the digitalis glucosides on the damaged heart varied considerably during the therapeutic stage depending upon the extent of the damage. This applied both to amplitude and minute volume. In preparations working under optimal conditions there was no therapeutic effect.

TOXIC EFFECT

With high concentration and rapid effect the amplitudes decreased gradually; the frequency remained constant and rhythm regular. Auricular and ventricular fibrillation then followed, and the heart then stopped, mostly in diastole.

In slow poisoning intermittent irritation and conduction disturbances occurred. Cushny's periodic variations were observed. Then followed intermittent flutter and fibrillation ending in death.

THE GLUCOSIDE CONSUMPTION OF THE HEART

Of the heart, lungs, and blood, the heart only showed a measurable affinity for the digitalis. It was found that the minimal lethal dose per gram heart was as follows:

Digitoxin	0.0046
G. Strophanthin	0.0020
Scillaren	0.0022

From experiments on the entire animal it was found that 9 per cent of the injected strophanthin was bound to the heart, 4.5 per cent of the scillaren. The digitoxin percentage lay between the two. The absolute effect on the isolated cat's heart was the same for G. Strophanthin and scillaren. For digitoxin it was only half that.

The next problem was, how much of the glucosides present in the blood did the heart absorb? It was found that when the calculated minimal lethal dose was present all the glucoside was taken up by the heart. If there was any more in the perfusion fluid at the beginning of the experiment, the surplus was still present at the end. The functional state of the heart did not influence the minimal lethal dose. Conclusion: For the warm-blooded animal the minimal lethal dose is also the absorption dose or effective dose. The dose is independent of the concentration of the glucoside.

From the literature it appears that the frog heart in room temperature can only be brought to asystole when one c.c. of the perfusion Ringer contains many times the consummation dose. Consequently a frog heart cannot completely remove the digitalis from a perfusion fluid. This is not true at lower temperatures. Conclusions: The heart muscle of all vertebrates is able to store digitalis glucosides.

The scillaren which was bound in the heart or which was present in blood (blood sample in ice chest) spontaneously disappeared. Digitoxin and strophanthin are not destroyed by the blood. The rate of action of digitalis glucosides is a direct function of the concentration.

Weese, H.: II. Digitalis Consumption and Digitalis Effect in Warmblooded Animals. Arch. f. exper. Path. u. Pharmakol. **141:** 329, 1929.

In this paper the author traces the fate of the digitalis glucosides which were not bound by the heart.

Especially musculature, liver, and kidney tissue preparations were examined, and these were shunted into a heart-lung preparation.

Muscle was found to absorb glucosides up to a certain point. It did not let any glucosides pass until it was completely saturated. After that glucosides were allowed to pass with the perfusion fluid. The time required for fixation is short, probably seconds.

The digitalis consumption of the liver is somewhat irregular, probably depending upon the fat content of the organ. But it does bind considerable amounts of glucosides. The conditions of absorption are similar to those found in the muscles.

Muscle and liver absorbed far less digitalis than the heart. The kidney was the only organ which bound a comparable amount of glucoside. The lungs bind no glucosides. The amount of glucoside bound by the muscle is in the summer 10 to 14 times, in the winter 5 times less than that bound by the heart. But as they exceed 50 per cent of the body weight, they nevertheless bind the greater part of administered glucoside. In absolute figures the liver and kidney also bind more glucoside than the heart.

If the dose of glucosides, which corresponds to the minimal lethal dose when injected intravenously, is injected into the aorta, then no digitalis reaches the large

veins. It is all bound in the body. The ability of the body, outside the heart, to absorb digitalis is 1.7 times the minimal lethal dose. Therefore, with an intravenous minimal lethal dose the heart only is saturated with glucoside, not the remainder of the body.

The conclusion is that all digitalis glucoside which leaves the heart is bound peripherally in the body and will be of no more benefit to the heart.

Next the authors investigated the relation between the rapidity of injection and the minimal lethal dose. The premises were: The effective dose of digitalis is constant with constant temperature and constant heart weight. The healthy heart can *only bind glucoside during the period of injection. Variations of intravenous minimal lethal dose depends upon variation in utilization of the glucoside contents of the blood.*

Digitalis binding in the heart primarily is by reversible adsorption, secondarily follows an irreversible fixation. Therefore, adsorption surface and adsorption time are factors which determine the amount of glucoside taken up. More digitalis is bound with increasing concentration, with slower perfusion rate. If these are equal, more strophanthin than digitoxin will be found. The absorption rate, therefore, is quicker for the water soluble strophanthin. The time factor seems more important than the concentration factor.

DIGITALIS ABSORPTION IN THE INSUFFICIENT HEART

Insufficient hearts respond to digitalis with greater ease than compensated hearts. Also slow intravenous injection produces a better effect without toxic side effects, than does rapid injection of larger doses. The general explanation of this increased response is that a sensitization to digitalis exists in the decompensated heart. The author reasons that in cardiac hypertrophy and dilation there is an increased cardiac surface and increased area of coronary circulation; that is, an increased absorption surface. In decompensation the dilated heart is unable to drive the blood out during systole. This blood containing glucosides remains longer in contact with the ventricular wall than in a healthy heart. The same delay occurs in the coronaries. Therefore in decompensation both absorption surface and absorption time will be increased. This favors increased utilization of digitalis. Also, the slower the injection of digitalis, the greater the utilization.

STANDARDIZATION

The accuracy of the cat infusion method varies between better than 10 (De Lind van Wyngearden) and less than 27 per cent. Though the method is subject to some criticism, it is of some value which, however, does not exceed that of the frog preparation. The only proper way to standardize digitalis for parenteral administration is by perfusion under circumstances where the heart is the only organ absorbing the drug and then to give the minimal lethal dose.

Weese, H.: III. On Digitalis Accumulation. Arch. f. exper. Path. u. Pharmakol. **150:** 14, 1930.

Problem: Does the glucoside which has been found outside the heart have any cardiac effect after it has been bound?

Cloetta found that muscle binds digitalis irreversibly, after which ferments split it into aglycone and sugar. The aglycone is carried by the blood to the heart, where it exerts its specific action and leads to accumulation. The author showed, however, that the accumulation was not caused by digitalis found outside the heart, but by that found in the heart itself. Intact cats were given a sublethal dose of digitoxin. From two to twelve days later a heart-lung preparation was made from these cats, and it was found the actual lethal dose now was equal to the calculated lethal dose for a fresh heart of the same weight, minus the amount

bound by the heart after the injection into the intact animal. This amount, however, gradually disappeared at the rate of 3 to 4 per cent of the minimal lethal dose per day.

The conclusion is that only the digitalis bound in the heart contributes to accumulation, that bound in the tissues is worthless.

Grollman, Arthur: The Action of Alcohol, Caffeine and Tobacco on the Cardiac Output (and Its Related Functions) of Normal Man. J. Pharmacol. & Exper. Therap. *39: 313, 1930.*

The present paper presents data on the changes in the pulse rate, blood pressure, oxygen consumption, arteriovenous oxygen difference and cardiac output which follow the use of alcohol, caffeine, and tobacco. The determinations were all carried out on normal young adults under basal conditions. Pulse rate determinations were made by radial palpation for one minute. Blood pressure records were obtained with the Tycos recording sphygmomanometer. Oxygen consumptions were determined with the Krogh spirometer. The determinations of the cardiac output were made by the use of acetylene gas as described by the author.

The administration of even small doses of alcohol to nondrinkers resulted in a psychic response characterized by a transient rise in pulse rate, blood pressure, and cardiac output with a drop in the arteriovenous oxygen difference. Where no psychic reaction was elicited as in moderate drinkers such changes did not occur. In such cases amounts of alcohol equivalent to 60 c.c. of whiskey showed no demonstrable changes in blood pressure, oxygen consumption, arteriovenous oxygen difference, or cardiac output with a change of only a few beats per minute in the pulse rate during the first half hour after its administration. Larger quantities of alcohol caused slight changes in the pulse rate with appreciable increases in the blood pressure and cardiac output.

Small doses of caffeine were without effect on the cardiavascular system. Larger doses caused, in most cases, a rise in the oxygen consumption, slight or no changes in the pulse rate, an increase in the arteriovenous oxygen difference, and a slight rise in the cardiac output.

Tobacco, when indulged in its usual forms in moderate amounts by habitual smokers, produced no demonstrable changes in blood pressure or cardiac output with only slight or no increase in the pulse rate. Excessive smoking or smoking of tobacco in unaccustomed forms resulted in very large rises in blood pressure and moderate increases in cardiac output. When the blood pressure changes were slight, the cardiac output changes were minimal or absent.

Marshall, E. K.: The Cardiac Output of Man. Medicine 9: 175, 1930.

In this Harvey Lecture, the author discusses briefly the various methods used at present in the determination of the output of the heart under experimental and clinical conditions. He describes principally the method developed by Grollman and himself. This consists of inhalation of acetylene gas, and the measurement of its absorption and distribution. He believes that the estimation of the cardiac output can be determined for normal individuals under the basal conditions with results as *satisfactory* as those derived from estimation of basal metabolism. Using the acetylene gas method, the error of determination in a series of 50 normal individuals was no more than plus or minus 0.3 liters per square meter of body surface.

The author believes that the position of the subject and posture is without considerable influence on the cardiac output, when basal conditions are established for the determination of the cardiac output. Determination of cardiac output following ingestion of food shows that there is marked increase directly proportionate to the amount of food eaten. He discusses the influence of emotional state

of the subject and of muscular exercise on the cardiac output. He believes that both these influences are very marked and produce extreme changes in cardiac output.

Howell, W. H., and McDonald, C. H.: Note on the Effect of Repeated Intravascular Injections of Heparin. Bull. Johns Hopkins Hosp. 46: 365, 1930.

Results of this study indicate that a daily injection in dogs of a relatively large dose of purified heparin for six consecutive days does not cause any change in the corpuscles of the blood or any significant change in the clotting time. There was no indication of a shortening of this time but rather a slight tendency toward lengthening. It seemed that the excess of heparin injected into the blood was removed in part, at least, through the kidneys.

Beneke, Rudolph: Factors Predisposing to Coronary Sclerosis. Ztschr. f. Kreislaufforsch. 22: 359, 1930.

The form and construction of blood vessels is determined by physical hydraulic processes. This holds true also of the construction of connective tissues. The direction of the fibers is determined by the direction of the pressure of the blood stream. In the vessels where the pressure is perpendicular on the axis of the vessel (e.g., the aorta) the connective tissue is arranged in rings. In vessels where the pressure is in the direction of the stream, the fibers run longitudinally (in the smaller arteries). The fibrous tissue of a valve of a vein runs longitudinally on the surface facing the blood current. Inside the pocket the direction is crosswise. It is concluded that every fiber of the body owes its direction to the pressure exerted upon it when it was formed.

Considering this principle in the blood vessels, it should be remembered that the blood current is made up of a number of partial currents exerting somewhat different pressures. The opinions of the origin of vascular degeneration are divided; some consider the lipoid changes in the intima primary, others consider medial degenerations primary. The author considers the two processes fundamentally different. They are both reactions to overstrain but occur from different causes. Sometimes the causes creating both act together and result in combined atherosclerosis. No sharp border can be drawn between the extents of the two processes, or between the physiological and the pathological wear and tear reaction. The lipoid intimal changes are produced by the lipoids of the blood which are precipitated out of the blood and pressed into the intima; this process is determined by the direction and the power of the blood current and by the vitality of the tissues. It is also determined by fibrosis of the underlying media and perhaps by toxic sensitization (nicotine infections?). Especially nicotine seems important for the development of coronary sclerosis, which is supposed to be common in smokers.

The intimal degeneration, however, is determined by a primary fibrosis of the media. This fibrosis is caused by the strain by the separate currents in the blood stream. These currents are determined as to direction and power by the forms of the vessels. The coronaries being naturally tortuous will create eddies which will strain their walls. This strain will be aggravated where the pressure is high as in hypertension. The mechanism of these currents is discussed somewhat in detail.

Alt, Howard L., Walker, George L., and Smith, W. Carter: The Cardiac Output in Heart Disease. II. Effect of Exercise on the Circulation in Patients with Chronic Rheumatic Valvular Disease, Subacute Rheumatic Fever and Complete Heart-Block. Arch. Int. Med. 45: 958, 1930.

Four normal subjects and seven patients with compensated heart disease were subjected to two moderate standardized grades of work on the Krogh bicycle

ergometer. Measurements were made of the cardiac output, pulse rate, blood pressure during exercise. The response of the cardiac output in the patients with heart disease was not essentially different from the response of normal subjects. The lowest values occurred in a youth in good physical training with mild valvular disease who performed the work with ease and in a young adult with complete heart-block, who performed the work with difficulty.

Four of the patients with heart disease experienced fatigue and dyspnea during exercise. Fatigue was usually more marked than dyspnea. The first patient had advanced aortic and mitral disease with marked cardiac enlargement. The pulse pressure which was abnormally high at rest increased relatively as in the normal subjects during exercise. The second patient, who had subacute rheumatic fever, had an abnormal increase in the pulse rate while the stroke volume did not rise above its basal level. In the third, a young woman with complete heart-block, the pulse rate doubled during exercise. This was effected both by an increase in the ventricular rate and by the occurrence of extrasystoles. The fourth patient, a young man with complete heart-block, had a slight decrease in the pulse rate during exercise. This was accompanied by a greatly increased stroke volume, higher than any previously reported in the literature. Both patients with complete heart-block had an unusual rise in the pulse pressure during work.

Sutton, D. C., and Lueth, Harold C.: Experimental Production of Pain on Excitation of the Heart and Great Vessels. Arch. Int. Med. 45: 827, 1930.

Symptoms analogous to those occurring in man in angina pectoris and coronary occlusion can be produced experimentally in the dog; namely pain, sometimes nausea and vomiting, stimultion of respiration and fall in blood pressure. By utilizing a method previously described for temporary occlusion of the coronary vessels in the unanesthetized dog and also methods for the production of pain and its transmission, the authors have found that compression of the artery, vein, and included tissue produces first a cyanosis of that portion of the ventricle supplied by the vessels; the vein becomes distended, while the myocardium becomes definitely paler. Almost immediately there is a definite and at times a marked increase in the volume of both ventricles, and later also of the auricles. Immediately following partial compression of the vessels there is a definite rapid fall in blood pressure, amounting to from 30 to 55 *mm. of mercury*. Marked irregularities of the heart appear and seem to be increased by anoxemia.

It is suggested that sudden death in angina pectoris may be the result of ventricular fibrillation occurring during temporary decrease in coronary flow.

Acute mechanical distention of the aortic arch, ascending aorta and aortic ring, and the cavity of the left ventricle does not produce pain in the dog. It does produce paroxysmal dyspnea. There may be either a rise in blood pressure or no definite change. Acute mechanical distention of aortic ring of the left ventricle invariably produces a fall in blood pressure even when both vagi are severed. Mechanical and electrical stimulation of the annulus of Vieussens after all vagal strands are severed invariably produces an increase in blood pressure.

Cannell, D. E.: Congenital Aneurysm of the Interventricular Septum. Am. J. Path. 6: 477, 1930.

The clinical and pathological findings in two cases with congenital aneurysm of the interventricular septum are reported. The absence of clinical signs and symptoms in both cases wherein marked distortion of the normal anatomy was present is remarkable.

Photographs of the specimens are included.

A critical study of these cases adds further evidence in favor of these anomalies being congenital malformations rather than the terminal results of endocarditis.

Burkhardt, E. A., Jr.: Marked Dilatation of the Left Auricle of the Heart. Am. J. Path. 6: 463, 1930.

A man, aged twenty-three years, was admitted with a diagnosis of chronic cardiac rheumatic valvular disease with auricular fibrillation with embolism of the left internal capsule and probable subacute bacterial endocarditis. Death occurred the following day.

Autopsy showed, aside from the usual findings in the heart, a left auricle which was markedly dilated, the right border extending 8 cm. to the right of the midclavicular line in the region of the fourth rib. The left border lay in the arch of the aorta. The auricle had a capacity of 593 c.c. of fluid after fixation. The mitral valve was stenosed to a slit-like opening. There was a mural thrombus within the left auricle.

Barnard, William G.: A Case of Paradoxical Embolism with Blood-Clot Lodged in Foramen Ovale. Quart. J. Med. 23: 305, 1930.

The patient, a well-nourished and well-developed man of sixty-three years, was under treatment for carcinoma of the prostate. A suprapubic cystostomy was performed and radium inserted into the growth. Recovery was satisfactory, and the patient was getting up at the end of a fortnight. On the sixteenth day, he was kept in bed on account of symptoms ascribed to indigestion. In the evening of that day he died quite suddenly, while talking to another patient.

At the post-mortem examination, a mass of coiled, mixed, red, pink and grey laminated clot with a rippled surface was found completely filling the right and left pulmonary arteries and extending for a short distance into their main branches. An entirely separate clot of similar formation and about 15 cm. long was caught in the foramen ovale in such a way that its greater length hung free in the left auricle and down into the left ventricle, while a much shorter, thicker part projected into the right auricle. It seemed that the clot in the foramen ovale was of a similar sort to that in the pulmonary artery and not a part broken off.

Photograph of the specimen is included in the report.

Cox, Ralph L.: Aneurysm of the Coronary Arteries. Am. J. M. Sc. 180: 37, 1930.

A case of aneurysm of the right coronary artery is reported. There were no clinical findings suggesting this lesion. In addition to the coronary aneurysm and to nodular inequalities in the circumferences of the medium-sized arteries, there was a large saccular aneurysm of the abdominal aorta and a fusiform aneurysm of the right common iliac artery. There was an extreme degree of sclerosis of the coronary arteries with occlusion of the left ramus descendens and extensive myocardial infarction.

Gilchrist, A. Rae, and Ritchie, W. T.: The Ventricular Complexes in Myocardial Infarction and Fibrosis. Quart. J. Med. 23: 273, 1930.

A study of 148 cases of serial electrocardiograms indicates that sequential alterations of the R-T segment and of T, occurring in the course of a short period of time are strong presumptive evidence of myocardial infarction. Similar changes developing more slowly may be observed apart from myocardial infarction and may be due to dystrophic myocardial fibrosis following chronic progressive coronary sclerosis. The evidence available at the present time does not lend support to the view that the form of the electrocardiographic distortion can be regarded as a definite localizing sign of the infarct.

Bach, Francis: On the Clinical Significance of Right Branch Bundle Block. Quart. J. Med. 23: 261, 1930.

Eighty cases of branch bundle block have been investigated clinically and electrocardiographically. They have been divided into three groups determined by the etiology of the lesion, namely, cardiovascular-degenerative, syphilitic, and rheumatic. The author believes that the clinical picture and the prognosis is different and distinct in these three groups.

In group one, consisting of fifty patients, ten have died since being under observation, fifteen are at present untraced, and twenty-five alive. In group two, of seventeen syphilitic cases, nine are already dead, four are untraced, and four are alive. In group three, of eleven rheumatic cases with mitral stenosis, one has died, seven are still attending the hospital and three are untraced.

Hyman, Albert S., and Parsonnet, Aaron E.: Bundle-Branch Block. The Phenomenon of Its Development in Relation to Axis Deviation of the Heart. Arch. Int. Med. 45: 868, 1930.

In a group of 469 cases showing left axial deviation of the heart the authors have studied 46 that show an upright QRS and a negative T-wave in Lead I and a downward QRS and an upright T-wave in Lead III. These cases have been followed for periods ranging from eight months to four years. Of the forty-six patients, twenty-one developed true right bundle-branch block with no change of sinus rhythm, and eight developed auricular fibrillation with bundle-branch block; four showed complete auricular and ventricular dissociation with bundle-branch block, and the remaining thirteen showed right bundle-branch block with an extrasystolic arrhythmia from single and multiple foci.

In this connection, the authors were able to watch one case of right axis deviation of the heart which developed into a true left bundle-branch block prior to the death of the patient. Considerable prognostic information may thus be secured from close scrutiny of all electrocardiograms taken during age periods mentioned in the study.

The onset of bundle-branch block may sometimes be suspected many months and even years prior to the actual development of the typical delayed conduction phenomena which are so characteristic of this condition.

Coombs, Carey F.: Observations on the Etiological Correspondence Between Anginal Pain and Cardiac Infarction. Quart. J. Med. 23: 233, 1930.

The author has studied a group of 86 cases in which cardiac pain persistent in character and not necessarily excited by effort was followed by evidence of gross injury to the wall of the heart; also a second group of cases in which the pain was excited by effort, relieved by its cessation, and not followed by a structural sequelae. The age and sex incidence of the two groups correspond closely with one another.

The angina of effort occurs principally in association with cardiac syphilis, high arterial tension and senile degeneration of the heart. Cardiac infarction occurred in the second and third of these three etiological groups but rarely in the first. Both syndromes are rare in the other infective and toxic diseases of the heart.

The author concludes that pain of an anginal kind is produced by those types of diseases which fail to forward oxygenated blood to the cardiac muscle.

Werley, G.: Coronary Infarct and Angina with Abdominal Symptoms. M. J. & Rec. 131: 367, 1930.

The author believes that coronary infarction is similar in its etiology to infarction which may occur in other parts of the body with pronounced symptoms of

pain. This is particularly true of infarction in the abdominal arteries. He believes that sclerosis of the arteries is a strong predisposing factor in the production of coronary infarction. He describes four cases that showed mesentery thrombosis or symptoms referable to the abdomen which might be differentiated from coronary infarction and angina.

The author believes there is little or no relation of cause and effect between gallstones and coronary sclerosis. In a series of 575 autopsies, there were 26 instances of cardiac infarction none of which showed signs of abdominal disease. He believes there may be a common cause between gallstones and coronary sclerosis, since cholesterol is the main constituent of both gallstones and the atheromatous plaques of arteriosclerosis; therefore, in patients showing arteriosclerosis there might be found some evidence of gallstones and cholecystitis.

The author discusses the possibility of angina pectoris being due to an allergic disturbance within the heart muscle. He points out that similar disturbances can occur in the lungs, abdomen, and other parts of the body associated with vasomotor changes. He also reports three cases of coronary infarction in which there was marked hematemesis.

Burton, J. A. G., Cowan, John, Kay, J. Hunter, Marshall, A. J., Rennie, J. K., Ramage, J. H., and Teacher, J. H.: Four Cases of Fibrosis of the Myocardium With Electrocardiographic and Post-Mortem Examinations. Quart. J. Med. **23:** 293, 1930.

Four cases of coronary artery disease are described with a history of cardiac ailment up to eight years. In the first case after the initial coronary occlusion with the usual symptoms, working capacity was maintained for seven years, then anginal attacks followed for six months, in one of which death occurred.

Electrocardiograms showed a type of T-wave inversion indicating infarction of the posterior ventricular wall. The inversion first observed thirty-seven days after the infarction had not disappeared six and one-half years later. The second, third, and fourth cases were similar in that there was a history of cardiac distress, edema, breathlessness, and gradual congestive failure resulting in death. In the second case the anterior coronary artery was almost occluded, and there was fibrosis in the muscle supplied. In the third case, the descending branch of the coronary artery was occluded, and there were patches of fibrosis in the ventricular wall. In the fourth case the descending branch of the left coronary artery was almost occluded, and the right coronary was markedly narrowed. There was dystrophic fibrosis in the left ventricular wall and part of the septum.

These cases were not associated with characteristic electrocardiographic changes.

Davies, H. Whitridge, and Holmes, Geoffrey: Some Effects of Warm Immersion Baths Upon the Circulation. Quart. J. Med. **23:** 327, 1930.

Detailed findings of pulse rate, blood pressure, circulaton rates and metabolism on three normal human subjects in fifteen different experimental baths are recorded. The pulse rate was increased, the systolic blood pressure either increased slightly or was maintained, while the diastolic blood pressure was reduced sometimes to a considerable extent. The circulation rate showed, as a rule, a small increase but was markedly reduced in two instances when considerable pulmonary hyperventilation and consequent gaseous alkalosis occurred.

Bohrod, Milton G.: Rheumatic Pericarditis With Polypoid Formations. Arch. Path. **10:** 51, 1930.

In the pericardium of a man twenty-seven years old with typical rheumatic heart disease, a peculiar polypoid mass was found. Clinical evidence of pericarditis had

never been observed. Necropsy disclosed an old mitral and aortic valvulitis with a recent endocarditis engrafted on this process. All the chambers were dilated, and hypertrophy occurred in the muscle. The heart with the pericardium weighed 1400 grams.

The unusual features were in the pericardium. There were adhesions between the pericardial layers in most places, fibrinous and easily broken, but in the region of the interventricular septum anteriorly the two layers were firmly bound together. About 75 or 100 c.c. of cloudy, slightly brownish fluid were found in the sac. Both layers were covered by shaggy fibrinous material easily stripped off. The color of the pericardium was chocolate brown.

At the reflection of the parietal pericardium from the right auricle posteriorly hung a large hydatidiform mass. The distal two-thirds of this mass were made up of several dozen bluish polypoid bodies from 4 to 15 mm. in diameter, a few of them solid but most of them filled with blood in various stages of inspissation. In some, the contents were thick and chocolate brown. From the posterior part of the mass hung a long loop of firm tissue 1.5 mm. thick. Over the surface of the auricle and underneath the auricular appendage there were tiny brownish projections from 0.5 to 3 mm. in length usually solid but occasionally cystic, the contents of the cysts being old blood.

Microscopically, the polypoid bodies were cysts with walls of varying thickness, lined by a single layer of flattened cells and filled with erythrocytes.

Detailed description of the specimen follows.

Perry, C. B.: The Main Branches of the Coronary Arteries in Acute Rheumatic Carditis. Quart. J. Med. 23: 241, 1930.

This investigation was incited by the discovery of severe intimal thickening in the main branches of the coronary arteries, considerably reducing their lumen, in a child with severe rheumatic carditis who during life suffered from typical anginal pain. In order to see whether these changes were exceptional or usual in this disease, blocks, which included the main coronary arteries, were taken from the next eight fatal cases of rheumatic carditis that were submitted to autopsy. All of these hearts showed changes in one or more of the main branches of the coronary artery which though less intense than those in the first case were essentially similar in nature. The lesion is a general panarteritis consisting of: (a) intimal thickening more or less cellular; (b) degenerative and inflammatory lesions of the media; (c) inflammatory infiltration and fibrosis of the adventitia.

Hill, N. Gray, and Allan, Mary: The Family Incidence of Juvenile Rheumatism. Brit. M. J. p. 949, May 24, 1930.

Information has been collected from the parents of 400 rheumatic children relating to the incidence of rheumatic manifestations in their families. Of the 400 families investigated, the total number of children was 2,156 and the total number of rheumatic children in these families was 540.

The present rather limited inquiry seems to indicate that very few of the brothers and sisters of the rheumatic patients developed the disease. The possibility is suggested that with more exhaustive inquiry made only after the entire family have passed the age of twenty-five years, an increased number of rheumatic members might be found.

In the series, there were eight pairs of twins and in not a single incidence have both twins developed recognizable manifestations of rheumatism. In only six families do both father and mother give a history of juvenile rheumatism, and in only a comparatively small number of incidences is there a history of rheumatism among both the father's and the mother's relatives.

Ernstene, A. Carlton: Erythrocyte Sedimentation. Plasma Fibrinogen and Leukocytosis as Indices of Rheumatic Infection. Am. J. M. Sc. **180:** 12, 1930.

The corrected sedimentation index, plasma fibrinogen content and leucocyte count were measured at frequent intervals in 22 patients with rheumatic fever. At the height of the illness the corrected sedimentation index showed a greater relative increase above normal than did the leucocyte count. Both the leucocyte count and the index were depressed somewhat by salicylates, but in general the sedimentation index seemed to be less affected than the white blood cell count. A slight increase in the leucocyte count and corrected sedimentation index followed by a prompt return to the previous level was observed frequently after discontinuance of salicylates.

With exacerbations of the infection in the polycyclic and continuous types of the disease, there was usually a greater relative increase in the corrected sedimentation index than in the leucocyte count. In all types of the disease, the index, with few exceptions, remained elevated for several days to a few weeks after the leucocyte count had become normal.

The author concludes that the corrected sedimentation index is a test preferable to estimations of the plasma fibrinogen content on account of its greater simplicity. He also believes that the rheumatic infection cannot be considered arrested until the corrected sedimentation index has become and remains normal.

Faulkner, James M.: The Significance of Sinus Arrhythmia in Old People. Am. J. M. Sc. **180:** 42, 1930.

The pathological significance of sinus arrhythmia in old people with organic heart disease is discussed. Case reports from four patients are presented. Analyses of hospital records show that sinus arrhythmia in patients over fifty years of age is more frequently associated with evidence of organic heart disease than is normal rhythm. Support is lent to the observation that sinus arrhythmia may at times represent a reflex response to abnormal efferent stimuli from a diseased heart or aorta.

Riseman, Joseph E. F., and Weiss, Soma: The Symptomatology of Arterial Hypertension. Am. J. M. Sc. **180:** 47, 1930.

An analysis of the complaints of 1,090 ambulatory patients with primary (essential) hypertension indicates that the following symptoms are present in more than 20 per cent of the cases: headache in 43.3 per cent, dizziness in 40.3 per cent, aches and pains in 38.7 per cent, dyspnea in 27.7 per cent, nycturia in 25.9 per cent.

Arterial hypertension is not associated with characteristic symptomatology. Almost all the symptoms of patients with arterial hypertension are referable to a disturbance of the central nervous system and are expressions of a disordered vasomotor system.

Among conditions with normal blood pressure, menopause, obesity, and psychoneurosis showed symptoms similar to those of arterial hypertension. All four conditions frequently exhibit vasomotor instability.

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The American Heart Journal

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